

# Newsletter

# Congratulations



**Laura Kilpatrick** has been awarded an Anne McLaren/Nottingham Research Fellowship from the University of Nottingham to commence in 2020. Laura has been an important member of Cell Signalling for the last ten years as research assistant, BPS A J Clark PhD Student and Postdoc.

The fellowship provides Laura with three years of independent funding and is linked to a permanent academic position in the School of Pharmacy. Although Laura will be moving from the School of Life Sciences to the School of Pharmacy, she will remain an important member of COMPARE and will now be eligible to be a full academic supervisor for our Wellcome Trust Four-Year PhD programme on

## Welcome

**Jason Mercer** joins the Institute of Microbiology and Infection at University of Birmingham and COMPARE as a PI. Jason joins us from UCL where he was Group Leader at the Laboratory for Molecular Cell Biology and a Reader in Viral Cell Biology. Throughout his scientific career Jason has been fascinated by the elegant simplicity of viruses.



During his PhD with Prof. Paula Traktman (Medical College of Wisconsin) he became interested in how poxviruses subvert cellular systems to build new viral particles. To further explore poxvirus host-cell interaction, Jason joined the lab of Professor Ari Helenius (ETH Zurich, Switzerland) for his postdoctoral training. As an EMBO postdoctoral fellow Jason discovered that poxviruses use a novel entry strategy termed viral apoptotic mimicry. In 2014, Jason was appointed as Associate Professor of Virus Cell Biology at the MRC Laboratory for Molecular Cell Biology (UCL). Supported by the MRC and a European Research Council Consolidator Award, Jason's lab strives to incorporate state-of-the-art technologies including advanced imaging (super-resolution microscopy) and analysis (artificial intelligence) to uncover novel mechanisms by which poxviruses subjugate host cell function.



**Mireia Jimenez Roses** has joined COMPARE working on the Veprintsev/Styles collaboration contributing to understanding GPCRs pharmacological ligands and bias signalling by computational approaches.

Mireia received her MSc degree in Structural Bioinformatics from the Universitat Autònoma de Barcelona (UAB) in 2015. She did her PhD in the Computational Medicine Lab at UAB (2015-2019) where she focussed on the understanding of the structure and function of G protein-coupled receptors (GPCRs) by applying computational chemistry techniques such as homology modelling, docking and molecular dynamics simulations.

#### Edition 22 January 2020

#### **Key Dates**

#### **Team Science Seminar**

Wednesday 29th January 2020 Chris Denning—UoN Emma Faulkner–UoB A208 Biodiscovery Institute, UoN

#### **Dual PhD Student Presentations**

Wednesday 26th February 2020 C2505, Medical School, Nottingham

Sandpit—Computational/AI/ Machine Learning Wednesday 11th March 2020 University of Birmingham

#### COMPARE Annual Research Symposium

24th September 2020 Edgbaston Park Hotel, Birmingham

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If you have any items for the next newsletter please send to:

compare@birminghamnottingham.ac.uk



# **Dual PhD Presentation Day**

COMPARE funded PhD students will be holding a presentation day at the University of Nottingham, with each student showcasing their project. The day will run from 11:00-16:00 followed by drinks and nibbles and will be held in C2505 of the Medical School, University of Nottingham.

Dr Graham Ladds will be joining us from the University of Cambridge and will be giving a guest lecture between 15:00-16:00 entitled: 'Factors influencing Family B GPCRs: RAMPing it up'.

All members of COMPARE are welcome to attend for the full day or for specific presentations throughout the day.

11:00-11:15	Arrival and Coffee
11:15-11:45	Insights gained from single-particle tracking of GPCR-beta arrestin dynamics in live cells. Jak Grimes
11:45-12:15	Development and applications of fluorescent ligands for GPVI. Fay Damaskinaki
12:15-12:45	Investigating a Gly138Val variant in GPIba and its potentially atypical role in inher- ited bleeding. Jack Yule
12:45-13:30	Lunch
13:30-14:00	Using advanced microscopy techniques to investigate the role of actin in the or- ganisation of Adenosine receptors. <b>Evie Garlick</b>
14:00-14:30	Exploring the haemodynamic effects of Adenosine A <sub>2</sub> receptor ligands in con- scious, freely moving rats. <b>Eddy Wragg</b>
14:30-15:00	Break
15:00-16:00	Guest Lecture—Dr Graham Ladds- University of Cambridge Factors influencing Family B GPCRs: RAMPing it up.
16:00-16:30	Drinks and Nibbles

Diary invites have been sent to all COMPARE members, please decline or accept as appropriate. We look forward to seeing you there and sharing our exciting research with the broader COMPARE community.

## Sandpit

Hold the date—Wednesday 11th March - Discussion focus—Computational/AI/Machine Learning



## **Publications**

Ast J, Arvaniti A, Fine NHF, Nasteska D, Ashford FB, Nicolson PLR, Nock SH, Hinds J, Garcia-Quintanilla L, Smith Stamataki Z, Koszegi Z, Bacon A, Jones BJ, Lucey MA, Sasaki CW, Campos J, Brill A, Pike JA, Khan AO, Poulter NS, S, Brierley DI, Hastoy B, Tomas A, D'Agostino G, Reimann F, Kavanagh DM, Watson S, Watson CN, Clifford H, Huissoon Lynn FC, Reissaus CA, Linnemann AK, D'Este E, Calebiro D, AP, Pollitt AY, Eble JA, Pratt G, Watson SP, Hughes CE, Trapp S, Johnsson K, Podewin T, Broichhagen J, Hodson DJ, (2020). Low dose Btk inhibitors selectively block platelet (2020). Super-resolution microscopy fluorescent probes reveal endogenous glucagon-like haematol.2019.218545. [Epub ahead of print] peptide-1 receptor distribution and dynamics. Nat Commun. doi: 10.1038/s41467-020-14309-w.

Calebiro D, Grimes J, (2020). G Protein-Coupled Receptor Bioluminescence Resonance Energy Transfer Assays and Pharmacology at the Single-Molecule Level. Annu Rev Fluorescent Microscopy. Methods Mol Biol. 2041:163-181. 10.1146/annurev-pharmtox-Pharmacol Toxicol. doi: 010919-023348. [Epub ahead of print]

Comeo E, Kindon ND, Soave M, Stoddart LA, Kilpatrick LE, redundant functions of the adapters Grb2 and Gads in Scammells PJ, Hill SJ, Kellam B, (2020). Subtype-Selective platelet (hem)ITAM signaling in mice. Platelets. doi: Fluorescent Ligands as Pharmacological Research Tools for 10.1080/09537104.2019.1709633. [Epub ahead of print] the Human Adenosine A2A Receptor. J Med Chem. 2020 Jan 9. doi: 10.1021/acs.jmedchem.9b01856. [Epub ahead of print]

Eschenbrenner E, Jouannet S, Clay D, Chaker J, Boucheix C, Dean CH, Henderson DJ, Sansom OJ, Kendall TJ, Boulter L Brou C, Tomlinson MG, Charrin S, Rubinstein E, (2020). (2020). Non-canonical Wnt signalling regulates scarring in TspanC8 tetraspanins differentially regulate ADAM10 biliary disease via the planar cell polarity receptors. Nat endocytosis and half-life. Life Sci Alliance. doi: 10.26508/ Commun. doi: 10.1038/s41467-020-14283-3. lsa.201900444. Print 2020 Jan.

Green HLH, Zuidscherwoude M, Alenazy F, Smith CW, Sheikh MO, West AMV, Frank MM, Wells L, Xu D, Bicknell Bender M, Thomas SG, (2020). SMIFH2 inhibition of R, Corbett KD, Esko JD, (2020). Proteomics-based screening platelets demonstrates a critical role for formin proteins in of the endothelial heparan sulfate interactome reveals platelet cytoskeletal dynamics. J Thromb Haemost. doi: that C-type lectin 14a (CLEC14A) is a heparin binding 10.1111/jth.14735. [Epub ahead of print]

compatible activation by CLEC-2. Haematologica. doi: 10.3324/

Soave M, Goulding J, Markus R, Hill SJ, Stoddart LA, (2020). Application of Fluorescent Purinoceptor Antagonists for

Vögtle T, Baig AA, Volz J, Duchow TB, Pleines I, Dütting S, Nitschke L, Watson SP, Nieswandt B, (2020). Critical

Wilson DH, Jarman EJ, Mellin RP, Wilson ML, Waddell SH, Tsokkou P, Younger NT, Raven A, Bhalla SR, Noll ATR, Olde Damink SW, Schaap FG, Chen P, Bates DO, Banales JM,

Sandoval DR, Gomez Toledo A, Painter CD, Tota EM, protein. J Biol Chem. doi: 10.1074/jbc.RA119.011639. [Epub ahead of print]

## Branding

Academic publications should conform to each paper's standard requirements but must acknowledge the funding source and equipment. Documents may need to be adjusted according to the nature of the document and individual organisations standard formatting. All publications must be uploaded to PURE in Birmingham.

The agreed form of words to be included into publications is:

"COMPARE University of Birmingham and University of Nottingham, Midlands" in addition to home University affiliation.

### **Conference Awards**

Well done to Evie Garlick, COMPARE PhD student, who won the oral presentation prize at the BPS Pharmacology 2019 meeting in Edinburgh and to Rachel Stapley, UoB PhD student, who won the Scientist in Training award for her presentation during the annual British Society of Haemostasis and Thrombosis (BSHT) Meeting held at Aston University.



Microscopes—NIKON N-SIM S

Microscope Officer: Deirdre Kavanagh

Structured Illumination Microscopy (SIM) can be performed on our <u>Nikon N-SIM S</u> at the University of Birmingham site. System specifications can be found on the COMPARE website.

Structured Illumination Microscopy (SIM) allows the user to observe living and fixed fluorescent samples at resolution greater than a standard fluorescent microscope. Imaging at this resolution can reveal structural organisation inside a cell that can be otherwise masked.

SIM utilises a pattern of light (stripes) to excite the sample. The position and orientation of the striped pattern is rotated and the resulting emission captured. A total of fifteen images are collected (5 phases and 3 rotations) for 3D-SIM and nine images (3 phases and 3 rotations) for 2D SIM and TIRF SIM. Interference between the sample emission and

the patterned excitation results in <u>Moiré fringes</u>. These Moiré fringes contain high-frequency information on the minute structures within the sample. The raw data is reconstructed using an algorithm to give a final super-resolved image. (115 nm in XY and 300 nm in Z depending on sample and wavelength).



Fifteen images acquired (5 phases and 3 rotations) for 3D



Nine images (3 phases and 3 rotations) for 2D SIM.



Fluorescent tubulin microfilaments in COS7 cell image using standard widefield microscopy (left) and super-resolution SIM (right). Image courtesy of <u>Dr Deirdre Kavanagh</u>,



The technique is capable of multi-colour imaging (405, 488, 561, 640 nm laser lines) and live super-resolution imaging. The pattern rotation required for SIM, limits the acquisition rate in comparison to a diffraction limited microscope. A novel pattern modulation technology developed by NIKON allows acquisition speeds of up to 15 fps (2D SIM) and 8 fps (3D SIM) enabling fast biological processes to be captured at twice the spatial resolution of conventional light microscopes.

The SIM system is also equipped with an emission image splitter (Cairn TwinCam) and two sCMOS cameras (Hamamatsu Flash4.0). When used the system is capable of true simultaneous two colour imaging (emission filter set for green/red, red/far red and green/far red).



Proplatelet formation from a mature megakaryocyte. Image courtesy of Dr <u>Steve Thomas</u>, Senior Lecturer in Cardiovascular Sciences, University of Birmingham.



Megakaryocyte nuclei. Image courtesy of Dr Chris Smith, PDRA in Cardiovascular Sciences, University of Birmingham.

# **Example references**

<u>Demmerle et al.</u>, Strategic and practical guidelines for successful structured illumination microscopy. Nature Protocols. 2017

<u>Poulter et al.</u>, Platelet actin nodules are podosome-like structures dependent on Wiskott–Aldrich syndrome protein and ARP2/3 complex. Nature Communications. 2015.

<u>Jost & Rainer</u>. Super-resolution Multidimensional Imaging with Structured Illumination Microscopy. Annual Reviews. 2013.