

### Team Science Committee Year Review

Welcome to the very first COMPARE Team Science Newsletter! This is going to be a twice yearly newsletter which aims to update all members of COMPARE on Team Science activities. As this is the inaugural newsletter, I will give a brief rundown on what has happened during the first year of COMPARE Team Science.



In May 2017 a group of 50 COMPARE early career researchers got together for the first Team Science Away Day. During this day, Dr Jeanette Woolard and Dr Natalie Poulter introduced us to the exciting concepts of Team Science, which they hoped could be implemented within COMPARE. This day was a great opportunity to learn about the research within COMPARE and to meet the people doing this work at the bench. The 2017/2018 Team Science Committee was formed which was comprised of three researchers from the University of Birmingham and four from the University of Nottingham.

After the Away Day, the Committee got started on planning the Team Science events calendar for the year. We felt that to help foster collaborations between the two Universities the early career researchers needed to get to know each other better and have a deeper understanding of the research carried out at both institutions. With some additional funding, we set up a Team Science seminar series, which gave six (three from each institute) researchers the opportunity to present their work at the reciprocal University. Each of these seminars were very well received and were a great way to foster the links between the Universities.

In November, 16 members of COMPARE had the opportunity to attend a media workshop run by the excellent Media Woman. This workshop focused on presentation skills both to the media and to a lay audience. The course facilitators had extensive experience of working in the media and it was a unique experience to get unbiased feedback on our presentation skills. The training day was very well received and even the more experienced presenters in the group took something from it.

COMPARE was officially launched in April 2018 by a keynote lecture given by Nobel Laureate Professor Brian Kobilka. Prior to the lecture, the Team Science Committee were asked to put together an early career researcher symposium. As this symposium was held the day after the British Pharmacological Society's 7<sup>th</sup> focused meeting on Cell Signalling, the symposium showcased researchers from both Universities and from the ONCORNET PhD training programme and also from externally submitted abstracts and it was attended by over 110 delegates from a range of institutions across the world. The quality of the presentations was very high and a great showcase for the research within COMPARE.

Much of the Team Science Committee's efforts focused on planning the 2018 Away Day which was held in May at the Old Ikon Gallery in Birmingham. As a Committee we decided to have the Away Day focus on two aspects of Team Science: collaboration and recognition. The day was attended by over 40 members of COMPARE and we started the day by hearing about the success of a Team Science funding collaborative project. Professor Jason Swedlow gave a really insightful presentation about his experiences in working collaboratively and setting up a network of UK based imaging scientists. This was followed by speed networking, sharing an interesting fact about ourselves in 60 seconds, this was a great way to at least to get to say 'hi' to a lot of new people. After this we split into pre-assigned groups for a speed grant-writing session after which each team presented their project. The judging panel were very impressed by the quality and diversity of the projects and ultimately awarded the best project to the use of CRISPR to engineer an optogenetic version of a chemokine receptor into mice (we did ask for the projects to be ambitious with an unlimited budget!). In the afternoon session we shifted focus onto authorship and the ethics around appropriately assigning authorship. This included a presentation from Elizabeth Moylan from the Committee on Publishing Ethics (COPE), a lively round-table discussion on various aspects of authorship and group discussions on various existing authorship guidelines. The Team Science Committee is now in the process of preparing a COMPARE specific set of authorship guidelines and we hope to make these available soon.

Overall, we have had a productive and exciting first year of COMPARE Team Science. We have provided a programme of events that has enabled early career researchers to get to know each other which we hope is the first step in producing effective collaborations between the two sites. On behalf of the 2017/2018 Team Science Committee I would like to say a huge thank you to Chris and Sharmaine for their invaluable admin support. I hope that the coming year will be as successful and early career researchers within COMPARE will continue to engage with Team Science.

Leigh Stoddart  
Chair, Team Science Committee 2017-2018

[birmingham-nottingham.ac.uk/compare](http://birmingham-nottingham.ac.uk/compare)



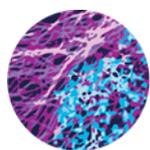
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**IN PARTNERSHIP:**

The Universities of Birmingham and Nottingham



## Microscopes—Olympus LV200 Livecyte—a bioluminescence microscope, Joëlle Goulding, University of Nottingham

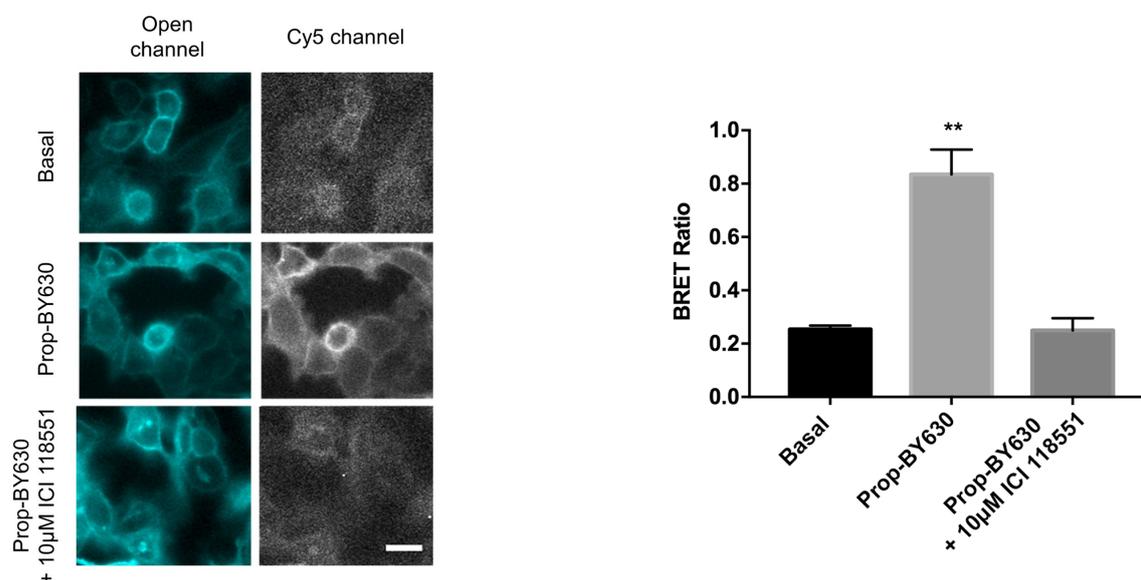
The Olympus LV200 is an inverted microscope setup which allows the imaging of bioluminescence. As there is no need to excite the sample as you would do in fluorescence imaging, bioluminescence offers improved signal-to-noise ratio and no phototoxicity nor photobleaching. The LV200 is encased in a light-tight dark box and there is minimal distance between your sample and the EM-CCD camera allowing maximal light collection and high-quality images. Due to this sensitivity image acquisition is fast allowing for the study of kinetics. The LV200 microscope is ideal for taking single cell bioluminescence readings and due to the environmental chamber samples can be imaged over longer time periods. Our system has the following objectives; 60xOil (1.42NA), 40xOil (1.3NA) 40x (0.6NA), 20x (0.75NA), 10x (0.4NA).

At Nottingham we have been working to develop BRET imaging on the LV200. BRET, Bioluminescence Resonance Energy Transfer, is the transfer of energy between a bioluminescent donor and a fluorescent acceptor in close proximity which lends itself perfectly to the study of receptor-ligand binding. We have combined the nanoluciferase technology as donor emitter with fluorescent ligands as acceptors.

This is exactly what Diana Alcobia, a final year PhD student within COMPARE at Nottingham has been doing. Diana has recently had her first, first-author paper 'Visualising ligand-binding to a GPCR in vivo using nanoBRET' published in iScience (vol 6. 31 August 2018, 280-288 <https://doi.org/10.1016/j.isci.2018.08.006>) combining work done in Nottingham, under the supervision of Professor Steve Hill, and in Monash Australia, under the supervision of Associate Professor Erica Sloan. Here she is giving her thoughts on the LV200;

"I found the LV200 luminescence imaging system very user friendly. This is an ideal system to complement our NanoBRET-based assays to measure ligand-receptor binding kinetics, as it allows the visualisation where specific ligand-receptor interactions are occurring within living cells. For instance,  $\beta$ -adrenergic antagonists (clinically known as beta-blockers) have shown therapeutic effect in preventing breast cancer invasion and metastasis. Using the LV200 microscope, we were able to determine the location of specific binding of a fluorescently-labelled  $\beta$ -adrenoceptor antagonist (Propranolol- $\beta$ -Ala- $\beta$ -Ala-X-BY630/650) to NanoLuc-tagged  $\beta_2$ -adrenoceptors overexpressed in triple negative breast cancer cells."

The LV200 figure from Diana's paper;

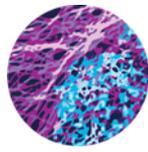


**Figure:** Bioluminescence imaging (Olympus LV200) of NanoLuc-tagged  $\beta_2$ -adrenoceptors. MDA-MB231HM Nluc- $\beta_2$ AR cells treated with 400nM furimazine substrate alone (upper panels) to detect luminescence in the absence of added fluorescent ligand using an open channel (20 sec exposure time; 420nm longpass filter; upper left panel) or a CY5 channel (4 min exposure time; 600/50nm bandpass filter; upper right panel); to detect BRET generated by binding of fluorescent ligand, when present). Middle and lower panels show images from cells treated with 50nM Prop-BY630, in the presence (lower panels) or absence (middle panels) of unlabelled ICI 118551 (10µM). Images shown were acquired with an open channel (middle and lower left panels) and the CY5 channel (middle and lower right panels). Scale bars represent 50µm.

**Graph:** BRET ratios obtained using bioluminescence imaging using ImageJ time-series analyser. Data show the mean and S.E. obtained in 3 independent experiments. \*\*  $p < 0.01$  compared to basal or in the presence of 10µM ICI 118551 (One Way ANOVA with Tukey multiple comparisons).

### IN PARTNERSHIP:

The Universities of Birmingham and Nottingham



# COMPARE

CENTRE OF MEMBRANE PROTEINS AND RECEPTORS

## Team Science Committee 2017—2018

### Chair

Leigh Stoddart leigh.stoddart@nottingham.ac.uk

### Committee

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## Team Science Committee 2018—2019

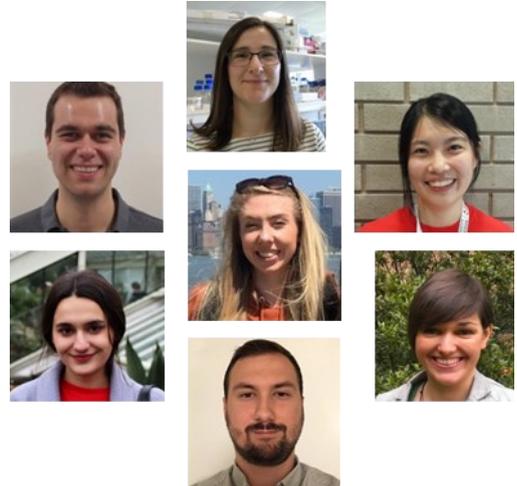
The new Team Science Committee from October 2018 will be as follows;

### Chair

Mark Soave mark.soave@nottingham.ac.uk

### Committee

Connie Koo chk543@student.bham.ac.uk  
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Vacancy University of Birmingham



## Team Science Funding

Applications will be invited for the Team Science Travel and Collaboration Grants in November 2018. Priority this year will be given to applications for collaborative projects between Birmingham and Nottingham, external collaborations, then travel grants.

### Support for collaborative projects or visits to a partner laboratory (max £2,000)

Applications for up to £2,000 are invited to support cross University research projects or visits to learn new techniques and skills that are within the scope of COMPARE. The money can be used to cover travel, consumables and equipment costs occurred during the visit.

### Support for Conference Attendance (max £500)

Applicants can apply for funds to support travel and registration at a conference. Applications will need to include details of how the conference fits into the scope of COMPARE and especially how it fulfils the Team Science objectives of fostering collaboration and career development.

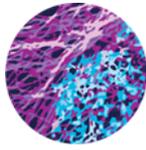
A post-award report and submission of an abstract and poster at the COMPARE Annual Research Symposium 2019, will be required from all successfully funded applicants.

Results will be known by mid-January 2019.

Further details on the application process will be circulated in November.

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## Post Funding Reports

Abdullah O. Khan, University of Birmingham, Carl White, University of Nottingham

### COMPARE Collaboration—Development of CRISPR PALM for quantitative single molecule imaging of CXCR4

The purpose of this project was to expand the CRISPR-PALM system we have under development at the University of Birmingham to the study of G protein-coupled receptors. Thus far, we can show a sequence dependent down-regulation of endogenously expressed photoswitchable tags in tubulin and Vimentin, and that optimised fluorophore design improves expression and the quality of any subsequent single molecule imaging. Carl has recently published on using CRISPR/Cas9 genome-engineering to investigate CXCR4 signalling by NanoBRET without the need for the donor luciferase to be over-expressed. GPCR signalling can be dependent on cellular context and localisation. Imaging techniques are frequently used to investigate these properties but can be confounded by the need to over-express the receptor of interest.

Therefore as we would like to expand the current work to look at the applicability of the CRISPR-PALM approach to single molecule quantification of a receptor, we established a collaboration (and joint Team Science application) to generate mEGFP, mEos 3.2, mEos 4b CO, and HaloTag CO knock-in cells. Interestingly while we have successfully generated HEK293 clones expressing CXCR4 tagged with mEGFP and HaloTag, we found mEos mis-folds on endogenous expression and aggregates. We are continuing with the work and are currently in the process of comparing quantitative data from our HaloTag experiments with overexpression vectors and functionally validating the knock in clones.

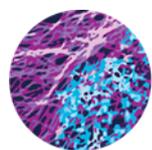
Meeting and establishing this aspect of the project between the Universities has been extremely informative for both of us. We came into this project with complimentary skills which we have been able, in part, to transfer to each other. There are a number of technical limitations in GPCR field which Carl has been able to demonstrate and troubleshoot (and that our work will hopefully address) and will be important considerations moving forward when applying these techniques to other membrane receptors. Conversely, Abdullah's expertise in PALM imaging has instructed and highlighted the technical challenges of these imaging techniques and these will be of vital importance for obtaining reliable quantitative single molecule imaging of CXCR4 in Carl's research going forward.

This has been an excellent opportunity to combine our complimentary skill sets and showcases the importance of Team Science collaborations. We have designed this project and developed it to cater to both our individual research needs, with the results obtained both immediately relevant to Abdullah's work, manuscript in preparation, as well as Carl's research going forward investigating CXCR4 stoichiometry with receptors under endogenous promotion.

The project was designed to benefit both of us by validating Abdullah's ongoing work and providing a validated tool-set for Carl's future work. Furthermore, the availability of Carl's existing donor designs and constructs from his previously published CXCR4 CRISPRs and his knowledge on CXCR4 in developing this end of the project has sped up the rate at which this project could have advanced. Abdullah's expertise in PALM imaging has allowed for the development, validation, imaging and analysis of the CXCR4-tagged cells lines, which would have previously been beyond the ability of Carl.

The data obtained from this work will contribute to a manuscript on which Abdullah is first author and going forward, Carl will have access to a number of cell lines which endogenously express CXCR4 with broad applications in single molecule imaging, single particle tracking, live cell imaging and FRET that will allow better understanding of receptor function.

We have gained grant writing experience and valuable data for an interesting project which is useful to both of us, and will hopefully open up avenues for a host of other projects. Similarly the experience of engaging in a collaborative manner with a colleagues from Nottingham and Birmingham has been very useful and the prospect of a manuscript is extremely valuable for both of our careers.



## Chloe Peach, University of Nottingham

### Laboratory visit: Professor Nigel Bunnett, Columbia University, New York

Discussions at the COMPARE Annual Research Symposium 2017 led to the visit to Columbia University to investigate collaboration and research opportunities. I presented a seminar to Professor Nigel Bunnett's laboratory group - my first international talk - enabling extensive discussion with high calibre scientists about my PhD project so far. This was followed by tours of the University's campus, as well as several meetings with Nigel and his group.



In addition to consolidating this relationship with Prof Bunnett, I spent time getting to know members of his lab group with some particularly interesting scientific discussions. This included Dane Jensen, a postdoctoral researcher who has worked with Nigel for numerous years on Protease Activated Receptors, as well as postdoctoral researcher Rocco Latorre with in vivo experience working with the GI tract physiology and first year graduate student Ariana Gavin working with opioid receptors. Despite I also met Assistant Prof Alex Thomsen recruited from the Leftkowitz lab who showed his structural work on megaplex formation. There was also an opportunity to spend time with Prof Meri Canals and Assistant Prof Rob Lane prior to their move to COMPARE in October. I was able to meet Prof Brian Schmidt, the Director of the Bluestone Centre of Clinical Research who specialises in head and neck cancer, as a long-term collaborator with Prof Bunnett based at New York University (NYU) with numerous joint NIH grants.

The Team Science initiative aims to harness collaborations across different fields of expertise, in terms of my PhD project, visiting Columbia University was extremely rewarding for widening my scope of impact, I gained insight from neuroscientists, physiologists and biologists. For example, based on their experience in endosomal signalling, they gave a new perspective on how VEGF could be degraded within endosomes. Presenting a talk also enabled me to promote the COMPARE and Team Science initiative on an international stage. In terms of Team Science, I witnessed first hand the benefit of collaborating across different disciplines (Chemistry, Clinical Sciences, Physics) and national/international institutions (NYU, University of Cambridge, multiple Australian universities, etc), leading to high impact papers and successful grant applications. This was also evident from their focussed scientific strategy, assortment of author institutions on publications and willingness to discuss collaborative ideas with our group.

Delivering a seminar to the Bunnett lab group at Columbia University was beneficial for both my professional and scientific development. I was able to discuss project directions and I was offered the opportunity for a postdoctoral position, partly dependent on funding, at a renowned and competitive university in the US. Discussing these prospects two years in advance of the end of my PhD means I can prepare and apply for postdoctoral fellowships and enables my training and interests to take shape towards my long term career goals in an interesting field that I wish to pursue an independent academic career in.

Laboratory visits present opportunities to meet with prospective colleagues and supervisors, you can discuss potential directions to see how much you would enjoy and benefit from that laboratory environment. I was able to build relationships beyond the University of Birmingham and University of Nottingham to those of the International Advisory Board and those visiting for seminars.

## Andrew Benest, University of Nottingham

### Conference: Vascular Biology and Human Diseases: From Molecular Pathways to Novel Therapeutics meeting, Santa Fe, New Mexico

Whilst at the conference I had the opportunity to present my recently submitted manuscript. I re-engaged with an old contact who will contribute additional data to my manuscript revisions. It also enabled me to agree a collaborative project with a group in the Neurology Institute in Frankfurt, Germany.

There were only two attendees from the UK, I was therefore able to raise the profile of Nottingham as a destination. Several people I met were positively encouraged to apply to Nottingham for research fellowships.

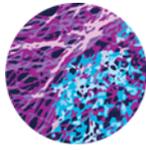


Attendance at the conference enabled me to present my work personally to two of my manuscripts reviewers, receiving personal feedback and encouragement to carry on and publish has been incredibly valuable. Moreover, how I can fund my own independent research niche from which I can build my own independent research career.

Our work in Nottingham is highly rated, and is within the 'new wave' of how angiogenesis related research is moving forwards vascular biology. This conference has demonstrated that as an independent research fellow I am welcome in the research community and can defend my own work to those that I need to see it.

## IN PARTNERSHIP:

The Universities of Birmingham and Nottingham



## David Sykes, University of Nottingham

### Conference: GPCR Structure and function: Taking GPCR Drug Development and Discovery to the Next Level, Santa Fe, New Mexico



I attended the Keystone conference 'GPCR Structure and function: Taking GPCR Drug Development and Discovery to the Next Level'. This conference highlighted the latest developments in GPCR structure/function and its contribution to the development of novel drugs. Many unique discovery methods were presented which will hopefully contribute to a period of more rational design. In addition this meeting highlighted the important role of intracellular signalling and its potential to impact modern drug discovery. The idea of allosteric networks or paths from the orthosteric binding pocket through to the intracellular face of the receptor where effector proteins bind was also introduced. This concept has direct consequences for biased pharmacology another area of research which was discussed in some detail. Understanding receptor bias is going to be extremely important as researchers strive to discover more selective therapies for chronic disease's where drug side effects are not so readily tolerated. Therefore methods for dissecting beneficial receptor activation pathways from side effect pathways is going to be another key area for modern drug discovery.

I interacted with a number of delegates at the meeting including several of the invited speakers and the meeting organisers. I met Bryan Roth who was very recently involved in crystallisation of the dopamine D2R and serotonin receptors. I have since followed up on these connections and provided a copy of my poster, which is concerned with the binding of antipsychotic drugs 5HT2A receptors and its contribution to side effect profile, to groups based in the US and Denmark increasing the chances of a useful collaboration in the future.

The groups in the US and Denmark are specialists in areas of GPCR research that complement our own interests/skills and therefore any future interactions have the potential to increase the quality of our own research output.

A deeper understanding of structural biology is crucial to the next phase of my professional development and my new position within COMPARE. This conference also provided an opportunity to see the latest developments in our understanding of the intricacies of receptor signalling-in terms of receptor-effector complex formation which was useful in stimulated thoughts around potential future grant opportunities.

The Keystone conference is regarded as one of the top meetings discussing GPCR pharmacology and structural biology but is sufficiently small to allow delegates the opportunity to meet the leaders in these fields in a very relaxed social setting.

## Elizabeth Haining, University of Birmingham

### Conference : Gordon Research Conference— Lymphatics for ECRs, Lucca, Italy

I attended the GRS Lymphatics 2018 conference. This meeting is the sister meeting to the larger GRC: Lymphatics meeting that directly followed and is organised and attended exclusively by ECRs.

The meeting included both oral and poster presentations (I presented a poster) across various themes within lymphatic research.

The entire meeting was a networking opportunity, and particularly as the posters were grouped such that people who worked in similar areas were together, I got the opportunity to meet and talk to people about their work that was very relevant to my own. I also met several people from the UK that also work in lymphatics, which has subsequently led to me to organise the first UK Lymphatic Science meeting scheduled to be held in Birmingham in 2019.

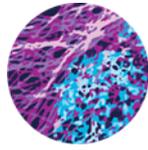
By attending an international scientific meeting that was run and attended exclusively by PhD students and early career researchers, it allowed dedicated time to interact with and develop professional links with my peers.

It also allowed me the opportunity to successfully apply to chair the next GRS lymphatics meeting. This position will give me a unique opportunity to gain experience in organising an international conference and also critically enhance my international visibility in the field.

As Chair of the next GRS meeting I will put the Team Science agenda at the heart of the 2020 meeting, so far as the Gordon conference organisation will allow. This will help to spread the Team Science message to the next generation of scientists in my field.

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The Universities of Birmingham and Nottingham



## Alexandra Matthews, University of Birmingham

### Conference: Regulation of the major platelet collagen receptor GPVI by ADAM10 and TspanC8 tetraspanins, Oracle, Arizona

The 9th International Tetraspanin Conference brought together experts from structural biology to single molecule imaging and physiology studies. Tetraspanins are a superfamily of 33 four-transmembrane proteins in mammals that interact with and regulate the intracellular trafficking, lateral mobility and clustering at the cell surface of specific partner proteins. Several invited speakers presented cutting-edge imaging techniques and new ideas for the tetraspanin field.

Dr Eric Rubinstein's laboratory researches the regulation of ADAM10 by TspanC8 tetraspanins and Dr Steve Blacklow's group has recently published the first crystal structures of a tetraspanin and the ADAM10 ectodomain. I was able to discuss the potential role that tetraspanins may play in regulating ADAM10 structure. I have previously collaborated with the van Spriel's group on the role of tetraspanin CD37 in CLEC-2-dependent dendritic cell migration. We have found that CLEC-2, a membrane hemiTAM receptor, and tetraspanin member CD37 interact, and these findings form part of a paper that is currently under review at the Journal of Cell Biology. This conference led to discussion of further experiments to progress the aforementioned project and the design of investigations to address reviewers comments in response to the submitted manuscript. Furthermore, as a side project, I have shown that CD82, the most closely related tetraspanin by protein sequence to CD37, also interacts with CLEC-2 and I was able to discuss these findings with Dr Miranti, the last person to publish a paper on platelet tetraspanin function.

The understanding of membrane proteins and receptors is central to COMPARE's goals and attending the tetraspanin conference enabled me to share my findings with other laboratories, network with other tetraspanin researchers, learn about new techniques employed in the field and shape my career development.

Several invited speakers presented data that has enhanced my understanding of the field and techniques used, as well as ground-breaking novel findings, including the first crystal structure of the ADAM10 ectodomain and how tetraspanins may regulate this. Furthermore, Dr Jennifer Gillette's Laboratory discussed use of a super-resolution imaging technique, dSTORM, which enabled me to discuss the clustering algorithms that could be applied to my experiments. The conference has ultimately provided me with alternative ways to address research questions and enabled my growth as a young researcher.

I have now decided to become a postdoctoral researcher and the conference has helped me to decide how to shape my scientific career.

## Joëlle Goulding, University of Nottingham

### Conference : BPS Cell Signalling 2018, Nottingham, UK

Cell Signalling is a bi-annual conference organised in collaboration with the British Pharmacological Society to discuss current developments in the field with a particular emphasis on GPCRs. This year it was held in Nottingham and it is attended by world-leading experts in the field of GPCRs/Cell Signalling.



As well as meeting new people from national and international institutions I was also able to network with scientists who I have met at previous related conferences. In particular I spoke at length with Dr Jacek Mokrosinski concerning his work in obesity and interest of the GloSensor assay I have previously worked with.

Attendance at this conference gave me opportunities to network, present my data, keep abreast of the field and reassess my work as to its relevance within my field.

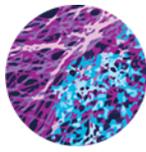
The invited talks were highly educational and gave a fantastic opportunity to learn about different disease systems and GPCR involvement.

The opportunity to attend this conference and keep abreast of new research and developments in the field is invaluable. Alongside this the chance to meet and discuss research with eminent scientists is fantastic.

I would recommend the BPS conference to my peers, as it is well organised and the speakers are thoughtfully chosen which results in a really stimulating two days of science.

## IN PARTNERSHIP:

The Universities of Birmingham and Nottingham



# COMPARE

CENTRE OF MEMBRANE PROTEINS AND RECEPTORS

## Samantha Cooper, University of Nottingham

### Conference: Experimental Biology 2018, San Diego, USA

This is an enormous conference hosted by five American societies (AAA, APS, ASBMB, ASIP and ASPET) who are comprised of more than 14,000 scientists. The areas of research presented at this meeting were vast. Primary areas of focus included: anatomy, biochemistry and molecular biology, investigative pathology, pharmacology and physiology. There were many opportunities to attend plenary and award lectures, workshops, oral and poster presentations, career services, networking events and exhibits.



There was a poster session every day, where up to 1000 posters were displayed. This provided opportunities to speak to researchers working in a similar field or in a field of interest. I met a number of people at these sessions, including Jamal Mustafa, who has carried out similar investigations to our group by investigating haemodynamic changes in adenosine receptor knock-out mice.

I was able to represent COMPARE at a large, international conference by presenting my work, which investigated regional haemodynamic responses to A2A adenosine receptor agonists. I also gained an insight into various cutting-edge scientific approaches in multiple fields, which are of high interest to COMPARE. Experiencing this has led to my group exploring new research/imaging methods, which may lead to high impact publications and may benefit COMPARE members in the future. I also interacted with a number of high-level researchers, which could lead to future collaborations.

By attending the conference I was given the opportunity to present my work at an international level and it was well received. I had many people stop by my poster, take an interest in my group's work and ask interesting questions. I attended a number of interesting seminars and keynote talks (e.g. by Michel Bouvier) and gained an insight into various novel and innovative scientific approaches in multiple fields, which has given me many ideas for future projects and new avenues to explore. Plus, the contacts I made whilst at EB could lead to future collaborations and partnerships with leading universities across the globe.

There were opportunities to attend career focused workshops, including the "Post-doctoral Colloquium: Tools and Tricks for Success in Science" and many more, which gave me an insight into maximising social media presence and how to effectively ask and answer questions.

I discovered new methods which can be used for in vivo imaging and now my group are planning to purchase the relevant imaging equipment, which will take our research on a new path and enhance my experimental tool kit. This has the potential to lead to high-impact research outputs.

## Rachel Richardson, University of Nottingham

### Conference: GPCR Structure and function: Taking GPCR Drug Development and Discovery to the Next Level, Santa Fe, New Mexico

This conference focused on molecular level structure and function of GPCRs. Including investigation of GPCR signaling networks, unraveling of structural details of GPCRs, their signaling partners and their signaling complexes. The study of these complex signaling networks have been enhanced through recent advances in the study of receptor conformation, and the role of receptor subcellular distribution in signaling efficacy, and this conference encompassed the use of new information and new techniques to present recent developments on this field.

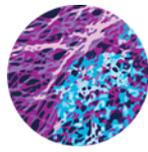
The poster sessions were very social and vibrant environments which enabled me to interact and discuss research with fellow scientists, and helped to foster conversations and networking opportunities.

As this conference was focused on GPCRs it is fundamentally related to the research goals of COMPARE which focuses on the research of membrane proteins and receptors. My attendance at this conference offered the chance to see and experience novel research and provided unique learning opportunities. In addition it allowed for the communication of science and the establishment of new collaborations and larger networks within science, thereby encompassing the aims and goals of COMPARE.

Attending the conference provided me with inspiration and motivation within my own PhD project and allowed me to network with other scientists in my field and to broaden my knowledge and network.

## IN PARTNERSHIP:

The Universities of Birmingham and Nottingham



## Outreach: Drug Discovery at Nottingham Academy

As part of an [IntoUniversity](#) Outreach programme, Chloe Peach, Nicola Dijon and Ellen Guest went into Nottingham Academy to introduce a class of Year 9 students to the field of pharmacology and drug discovery. This aimed to expose school pupils interested in medicinal sciences to alternative careers to medicine. This also gave us an opportunity to publicise our work to the community and show what research scientists do. Reflecting the interdisciplinary nature of drug discovery, this included *in vitro* pharmacologists Chloe and Nicola from the Cell Signalling Research Group (*School of Life Sciences*) as well as Ellen, a computational chemist partly sponsored by GlaxoSmithKline working on modelling protein-ligand interactions in the Hirst group (*School of Chemistry*).



The session began with an activity guessing everyday objects from electron microscopy images obtained from the UoN Nanoscale and Microscale Research Centre (nmRC) by Matt Wadge, a PhD student working on biomedical materials (*School of Engineering*). This was followed by an introduction to what pharmacology is and how drug discovery research works, building on the small scale of cells that can be seen by microscopes.

There were then three interactive stations covering: (1) the **drug discovery pipeline** and animal research; (2) a practical using **fluorescent proteins** seeing which objects fluoresce under UV light (including rhodamine fluorophores, a kiwi fruit, honey, images drawn with 'invisible ink', etc.), with special thanks to advice from the *School of Life Sciences Imaging (SLIM) team*; and (3) common **pharmaceutical drugs**, matching drugs to symptoms and side effects.

Students were then given the opportunity to ask us questions on post-it notes, which had an impressive range from "what do we enjoy about working in the lab" to "why can certain chemicals can both help and harm people". Having also asked whether we had ever made an approved drug during our PhD studies, they were unsurprisingly shocked by the average time and cost taken for a drug to get approved. It was an enjoyable experience, particularly with students that clearly engaged and had insightful discussions about research. As a class of teenagers, it was also interesting to realise what will and will not engage them about science. It certainly reminded us of the 'big picture' of why we do this research as this is often forgotten day-to-day, but fundamentally gave the next generation of potential scientists an opportunity to engage with the drug discovery field from female scientists in STEM.

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BRITISH  
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## COMPARE Team Science Publications

Matthews AL, Koo CZ, Szyroka J, Harrison N, Kanhere A, Tomlinson MG, 2018. Regulation of Leukocytes by TspanC8 Tetraspanins and the "Molecular Scissor" ADAM10. *Front Immunol.* 9: 1451

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Peach CJ, Kilpatrick LE, Friedman-Ohana R, Zimmerman K, Robers MB, Wood KV, Woolard J, Hill SJ, (2018). Real-time ligand binding of fluorescent VEGF-A isoforms that discriminate between VEGFR2 and NRP1 in living cells. *Cell Chemical Biology.* <https://doi.org/10.1016/j.chembiol.2018.06.012>

Soave M, Cseke G, Hutchings CJ, Brown AJH, Woolard J, Hill SJ, (2018). A monoclonal antibody raised against a thermo-stabilised  $\beta$ 1-adrenoceptor interacts with extracellular loop 2 and acts as a negative allosteric modulator of a sub-set of  $\beta$ 1-adrenoceptors expressed in stable cell lines. *Biochem. Pharmacol.* 147: 38-54