2019 WWIEM Summer Research Projects (*subject to funding)*

Code	PI Host lab & Contact	Website	Title	Project Summary
19A	**Dr Bettina Schock** b.schock@qub.ac.uk 	https://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/DrBettinaSchock/ https://pure.qub.ac.uk/portal/en/persons/bettina-schock(33bacb04-eff5-4d28-a477-f2746d0745d8).html	Role of IRG1 and itaconate on A20 expression in CF airways inflammation	Despite new drugs for cystic fibrosis (CF), CF patients suffer from persistent inflammation, which is driven by a lack of the NF-kB regulator A20 (Kelly *et al*. 2013). Inflammation activates mitochondrial respiration (Krebs Cycle) to provide ATP for the inflammatory response. Here, cis-aconitate decarboxylase (gene ACOD1/IRG1) produces anti-inflammatory itaconate (*cis*-aconitate + H^+ = CO_2 + itaconate (Michelucci *et al*. 2013)) and also stimulates A20 expression via reactive oxygen species (ROS) (Li *et al.* 2013). However, expression and function of itaconate in CF airways inflammation are not known. Taken together, we hypothesise, that reduced IRG1 contributes to the reduced expression of A20 in CF airway epithelial cells. We will use LPS-stimulated CF and non-CF airway epithelial cells (16HBE14o-/CFBE41o-) and (1) determine IRG1 mRNA and protein expression (qPCR/Western Blotting) and (2) inhibit IRG1 (CORM-2 {1µM plus H_2O_2}) and determine A20 mRNA expression and pro-inflammatory IL-8 (ELISA).
19B	**Dr Bettina Schock** b.schock@qub.ac.uk 	https://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/DrBettinaSchock/ https://pure.qub.ac.uk/portal/en/persons/bettina-schock(33bacb04-eff5-4d28-a477-f2746d0745d8).html	Glucose metabolism and anti-inflammatory itaconate CF airways inflammation	Despite new drugs for cystic fibrosis (CF), CF patients suffer from persistent airways infection and inflammation. Inflammation induces temporary hyperglycaemia (Smallwood et al. 2017) and increased Krebs Cycle activation (succinate) to drive inflammation. Itaconate is an anti-inflammatory metabolite of the Krebs Cycle, which inhibits succinate, mitochondrial respiration, and cytokines (Lampropoulou et al. 2016), but expression and function of itaconate in CF airways inflammation are not known. Preliminary data suggest higher glucose metabolism (↑ HK1 and PKM2) in CF airway epithelial cells. We therefore hypothesise that dysregulated levels of anti-inflammatory itaconate will contribute to the pro-inflammatory CF phenotype. Using an established model of high glucose exposure in cell culture, we wish to determine the levels of itaconate, IRG1 and succinate in CF compared to non-CF airway epithelial cells. The student will be using sterile working techniques, cell culture, mRNA and protein analyses and a colorimetric enzymatic assay to determine succinate levels.

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19C	**Dr Bianca Plouffe** b.plouffe@qub.ac.uk  **& Prof Jose Bengoechea**	https://pure.qub.ac.uk/portal/en/persons/bianca-plouffe(0be7b2ee-f281-4cd0-a490-a221c2f6009c).html	Non-canonical G protein signalling: toward a new generation of pharmacological treatments	Hormones can be compared to keys binding to cell surface receptors (locks). When this happens, proteins detecting this opened lock (called G proteins) are activated at the cell surface leading to specific cellular outcomes followed by receptor internalisation and signalling arrest. Recently, world-wide research teams discovered that for some receptors, G proteins are active intracellularly after receptor internalisation. These signals from intracellular compartments, termed as non-canonical G protein signalling (NCGS) are encoded differently and mediate unique physiological outcomes therapeutically exploitable. The student will have the unique opportunity to explore NCGS through a wide variety of cutting-edge molecular tools and will benefit from training in the new state-of-art Centre for Experimental Medicine. This project is particularly exciting and self-rewarding as a better understanding of molecular mechanisms underlying NCGS will lead to a new generation of treatments to fight diseases involving NCGS, such as cancer, heart diseases, diabetes, and chronic pain.
19D	**Dr David Grieve** d.grieve@qub.ac.uk 	http://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/Dr-David-Grieve/ https://pure.qub.ac.uk/portal/en/persons/david-grieve(62695a06-44b7-40c4-a0fe-9901afa735b7).html	INVESTIGATING THE INFLUENCE OF OXIDATIVE STRESS ON ENDOTHELIAL PROGENITOR CELL FUNCTION	Impaired angiogenesis influences the progression of cardiovascular disease and this project aims to investigate specific effects of oxidative stress and NADPH oxidases on endothelial progenitor cells (EPCs) which are known to play an important role in this process. In order to address this question, cultured EPCs will be treated with pro-oxidant compounds in the presence/absence of specific inhibitors of candidate pathways or after genetic manipulation prior to quantification of key signalling genes by real-time RT-PCR and/or western blot and in vitro functional assays. This project will provide the student with training in several techniques routinely used in pharmaceutical and biomedical research and first-hand experience of a multi-disciplinary research centre working alongside career academic scientists and researchers. It is hoped that the results will identify key pathways which may become dysregulated in disease and could represent potential targets to enhance the reparative capacity of EPCs and thereby increase their therapeutic potential.

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19E	**Dr Derek Brazil** d.brazil@qub.ac.uk 	https://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/Dr-Derek-Brazil/ https://pure.qub.ac.uk/portal/en/persons/derek-brazil(03a1cbf8-7d4e-4e2a-8269-5ffbe1830654).html	Uncovering the mechanisms of Gremlin1 signalling in colorectal cancer and kidney fibrosis	We work on Gremlin1, a secreted protein antagonist that inhibits bone morphogenetic protein signalling in a range of cells. Levels of Grem1 are high in many diseases, including fibrosis of the kidney, liver and lungs. Recent data has shown that high levels of Grem1 expression drives excessive cell growth in the intestine, and is associated with an inherited form of colon cancer called HMPS. Grem1 therefore represents an attractive novel target in the treatment of a range of human diseases. This project will involve the student joining a team of researchers deciphering Grem1 signalling using a range of cell culture models. Methods such as Western blotting, ELISA and fluorescence microscopy will be used during the project. The student will be exposed to cutting-edge research in the Brazil laboratory that has hosted previous winners of the CEM Summer Student Symposium 2016 and 2017.
19F	**Dr Gunnar Schroeder** g.schroeder@qub.ac.uk 	https://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/Dr-Gunnar-schroeder/ https://pure.qub.ac.uk/portal/en/persons/gunnar-neels-schroeder(d50dbee5-993f-48f5-85cd-6e96aeab7ad7).html	Dissection of effector protein function in the subversion of host cells by the respiratory pathogen *Legionella pneumophila*	*Legionella pneumophila* is a bacterial pathogen, which causes a potentially fatal pneumonia, called Legionnaires' disease. Key to the virulence of *L. pneumophila* is the injection of an extraordinary arsenal of 300 effector proteins, more than any other known pathogen, into host cells in order to enter and exploit them as replicative niche. The functions of the majority of these effectors are unknown. This exciting project will contribute to ongoing research in the Schroeder Team, which aims to characterise the function of a new effector family in the manipulation of cell-autonomous, innate immune defences in macrophages. Working at the host-pathogen interface, you will have the opportunity to get hands-on experience in a wide variety of experimental techniques, e.g. cloning of plasmids, transformation and culture of *E. coli* and *L. pneumophila*, mammalian cell culture and transfection and/or infection assays, which will be analysed by Western Blotting and/or fluorescence microscopy.

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19G	**Dr Imre Lengyel** i.lengyel@qub.ac.uk 	http://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/DrImreLengyel/ https://pure.qub.ac.uk/portal/en/persons/imre-lengyel(22d06c55-3707-4db3-b04e-4ce2f6630219).html	Expression of zinc transporters in cells and tissues of the eye	Zinc plays a pivotal, though still not well understood, role in how cells in the eye function. In this project we aim to map the expression and distribution of zinc transporter and binding proteins and their genes in cell cultures, human eyes as well as animal model eyes. The student will learn how to culture cells, section eye tissues and then isolate RNA to conduct qPCR experiments and visualize the location of relevant proteins using light and confocal microscopy. Based on these information there is a plan to use the recently installed laser capture microdissection microscope to isolate highly localised cellular events in tissues.
19H	**Prof Jose Bengoechea** j.bengoechea@qub.ac.uk 	https://pure.qub.ac.uk/portal/en/persons/jose-bengoechea(8a4317fc-ec60-4f46-9767-c1830461bc16).html	*Klebsiella* anti-immunology: deciphering how a multidrug resistant pathogen overruns the host	Antimicrobial resistance is one of the major health problems currently faced by humankind. We work to find new therapies by targeting the signalling pathways manipulated by pathogens. This requires in-depth knowledge of the complex relations between pathogens and the human host. In this project, we will investigate the interaction between *Klebsiella spp,* recognized as an urgent threat to human health by WHO, and the innate immune system. The student will investigate how *Klebsiella spp* attenuate host defence responses in macrophages by using established high throughput screens based on detecting the intracellular replication of the pathogen, and the activation of inflammation. The student will become familiar with tissue culture, ELISA, real time qPCR, confocal microscopy, and molecular microbiology (construction of mutants), and will receive mentorship to develop her/his presentation skills. The student will become an active member of the Bengoechea laboratory participating in weekly laboratory meetings and journal clubs.

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19I	**Dr Karim Dib** k.dib@qub.ac.uk 	http://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/DrKarimDib/ https://pure.qub.ac.uk/portal/en/persons/karim-dib(d580b715-c115-467c-b526-4cd63e90ecf5).html	To investigate the role of histamine in the regulation of neutrophil phagocytosis	Neutrophils constitute the first line of defence against bacteria and fungi. Neutrophils migrate to the site of infection where they capture and kill pathogens by means of phagocytosis. In many chronic lung diseases, histamine accumulates in lung fluids and tissues. Whether histamine plays a role in the clearance of pathogens by neutrophils is not known. We hypothesise that histamine is produced by bacteria and this substance blocks the ability of neutrophils to kill ingested pathogens. The action of histamine on neutrophils could be mediated via the histamine four receptor. By using antagonists of the histamine four receptor, we will investigate whether histamine negatively regulates neutrophil phagocytosis (bacteria killing) and whether histamine and histamine four receptor antagonists modulate the survival of *Galleria mellonella* (a wax worm model) infected with *S. aureus* or *P. aeruginosa*. We will also investigate whether bacteria produce histamine when they infect *Galleria mellonella*.
19J	**Dr Mei Chen** m.chen@qub.ac.uk 	http://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/DrMeiChen/ https://pure.qub.ac.uk/portal/en/persons/mei-chen(235fd081-5a43-4146-bf76-09308e61b0ab).html	Identifying novel cell types contributing to retinal fibrosis	Age-related macular degeneration (AMD) is a leading cause of blindness in the aged populations. There are two types of AMD: wet or neovascular type (nAMD) and dry or Geographic atrophy type of AMD. Anti-VEGF has been used to treat nAMD, however more than half of nAMD patients may develop macular fibrosis even with intravitreal injection of anti-VEGF. The fibrotic scar damage macular and cause irreversible visual loss. The underlying mechanism of macular fibrosis secondary to AMD is poorly defined and currently there is no medication to prevent or treat the conditions. In this summer studentship project, we wish to identify cell types in the fibrotic tissues of nAMD using a range of laboratory techniques including tissue sectioning, immunohistochemistry, immunofluorescence staining and microscopy. The student will have the opportunity to gain experience and confidence in organising lab based experiments.

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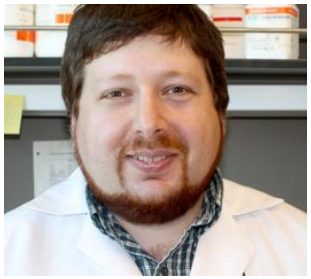
19K	**Dr Peter Barabas** p.barabas@qub.ac.uk  **& Prof Tim Curtis**	https://www.researchgate.net/profile/Peter_Barabas https://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/Professor-Tim-Curtis/ https://pure.qub.ac.uk/portal/en/persons/tim-curtis(305a269c-088f-4d57-bc15-6f4b55a357b2).html	Neurovascular changes in diabetic retinopathy	The prospective student will join a growing group of researchers studying diabetic retinopathy. We are interested in mapping how the neurovascular unit is remodelled in mouse models of diabetic retinopathy. The student will take part in this work through learning to do histological work and help characterize protein and peptide expression profiles in normal and diabetic retinas. Through this lab-based project, the student will gain insight into diabetes research and attain a better understanding of mouse eye anatomy, immunohistochemistry as well as the strength and limits of mouse models in biomedical research. The acquired wet lab skills will include: making buffers, dilutions, use of a pH meter, basic histology skills including fixing tissues for embedding, cryosectioning, immunohistochemistry, confocal laser scanning microscopy.
19L	**Dr Yvonne Dombrowski** y.dombrowski@qub.ac.uk 	http://www.qub.ac.uk/schools/mdbs/Research/MeetourResearchers/DrYvonneDombrowski/ https://pure.qub.ac.uk/portal/en/persons/yvonne-dombrowski(b281b2f8-118a-4bbd-b5c7-48b92b323c28).html https://en-gb.facebook.com/thedombrowskilab/ Twitter: @DombrowskiQUB	Identifying novel therapeutic targets of the innate immune system for brain repair in Multiple Sclerosis	Myelin is the protecting sheath around neurons that facilitates nerve signalling. Damage to this structure (=demyelination) can have devastating outcomes such as permanent disability. Currently, there is no cure for demyelinating diseases such as Multiple Sclerosis (MS). We identify novel therapeutic targets that can be used to repair myelin damage in MS. Inflammasomes are protein complexes that process the pro-inflammatory cytokine IL-1beta known to drive inflammation and disease pathogenesis. However, tissue repair is also to some extend dependent on inflammation. To date it is not known if inflammasomes play a role in brain repair. This project aims to understand the role of inflammasomes in myelin repair in an animal model of MS, which could have implications for the development of future therapeutics for MS. Students will learn murine tissue dissection, immunofluorescent staining, confocal microscopy, image analysis and immunoblotting as well as transferable skills such as project/time management and communication skills.