2024 WWIEM SUMMER RESEARCH PROJECTS

QUEEN'S UNIVERSITY BELFAST | WELLCOME-WOLFSON INSTITUTE FOR EXPERIMENTAL MEDICINE

Program Information: https://www.qub.ac.uk/research-centres/wwiem/EducationandTraining/SummerStudentProgramme/

Apply at: https://forms.gle/yJqDRbCN7EdafMqa7

Email: cemsummerstudents@qub.ac.uk

Program Coordinator: Dr Rebecca Coll

***Project code is required for the application form.** ****LB=laboratory-based**

PROJECT CODE*	SUPERVISOR	PROJECT TITLE	PROJECT DESCRIPTION	LB**	RESEARCH GROUP/PI WEBSITE
P01	Dr Imre Lengyel i.lengyel@qub.ac.uk	Softening the blow of mineralisation in age-related macular degeneration and Alzheimer's disease	Our research has three pillars: 1) Basic Research, 2) Clinical collaborations, and 3) Translational work. We established an interdisciplinary program to build a firm foundation for these three pillars with the final aim of helping to deliver better patient care. This summer studentship will support our recently funded program on soft tissue calcification in the eye and the brain. This program uses cell and molecular biology, human imaging and working with tissue sections. We will apply light, fluorescence and electron microscopic imaging of tissues and cells and correlate the findings with images from live human volunteers. The successful student will learn cell culturing, handling, and generating tissue sections labelled with specific protein, mineral, and lipid compounds to help visualise pathological pathways in the eye and the brain. This project is particularly suitable for applicants with a broad interest in biological sciences.	YES	https://pure.qub.ac.uk/en/persons/imre-lengyel
P02	Dr Bianca Plouffe b.plouffe@qub.ac.uk	Investigating the role of secreted Frizzled-related protein 2 in diabetic retinopathy	Diabetic retinopathy (DR) is a complication of diabetes mellitus causing chronic neovascularisation of the retina leading to blindness. Current treatments cannot provide long-term vision improvement or stability, which highlights the need for better treatments. Hyperglycaemic environment induces biological changes in retina Müller glial cells and contribute to DR development. Our preliminary data suggest that secreted frizzled-related protein 2 (SFRP2) is upregulated in Müller cells exposed to hyperglycaemic environment. As SFRP2 promotes angiogenesis in the context of several types of tumours, we believe that this protein represents a new therapeutic target for DR. The student in charge of this project will have the opportunity to develop important experimental competences and skills (cell culture, transfection, confocal microscopy, cell-based assays) and valuable knowledge of cellular signalling highly relevant to a career in biomedical research. This project is important and exciting as it may lead to an alternative treatment for patients suffering from DR.	YES	https://pure.qub.ac.uk/en/persons/bianca-plouffe
P03	Dr Bettina Schock b.schock@qub.ac.uk	The effect of pharmacological reduction of epithelial HE4 on SSc-ILD fibroblasts	In systemic sclerosis, 30% of patients develop interstitial lung disease (SSc-ILD) as a complication. SSc-ILD is characterised by pulmonary fibrosis (PF) with very limited treatment options. Our work so far suggests that hypoxia induced HE4 in airway epithelial cells, plays a key role in collagen production from lung fibroblasts. Importantly we can pharmacologically reduce HE4 from airway epithelial cells. Furthermore, we have iPSC derived fibroblasts from patients with SSc, SSc-ILD and healthy controls. In this project you will investigate the effect of HE4 reduction (in conditioned medium from treated epithelial) has on collagen deposition and inflammation of patient derived fibroblasts. Techniques you will learn include sterile working, cell culture of human lung fibroblasts, protein overexpression, analyses of HE4 (ELISA, (Western Blotting, qRT-PCR) and collagen (Western Blotting, Sirius Red	YES	https://pure.qub.ac.uk/en/persons/bettina-schock

			staining). Additionally, you will become proficient in presentations and teamwork and can present your work at a national respiratory meeting.		
P04	Prof. Jose Bengoechea j.bengoechea@qub.ac.uk	Discovering new antibacterial drugs by miming the antimicrobial effectors of the type VI secretion system	Bacteria use the T6SS to antagonize each other by injecting toxins into the target competitor. The human pathogen Klebsiella pneumoniae encodes one of such systems. We have shown that the number of Klebsiella T6SS toxins is far more comprehensive than anticipated. Many toxins have function that could not be predicted, suggesting that new antibacterial activities are to be found. The project is designed to characterize in a high-throughput manner using a quantitative luminescence-based method the antimicrobial effect of a collection of toxins from 100 strains representative of Klebsiella genetic diversity. Next, we will characterize the mode of action of one toxin using genetic and biochemical methods. The student will acquire expertise in the manipulation of biosafety 2 bacterial pathogens, practical knowledge on running high-throughput screens, and hands-on expertise on characterizing toxins enzymatic activity. These skills are highly sought by pharma. The student will participate in all the laboratory activities.	YES	https://pure.qub.ac.uk/en/persons/iose-bengoechea
P05	Dr Rebecca Coll r.coll@qub.ac.uk	Examining the function of CARD16 as a regulator inflammasome signalling in the human innate immune system	Inflammasomes are intracellular protein complexes that form part of the innate immune response to infection and injury. Inflammasomes trigger the secretion of inflammatory cytokines (IL-1β) and cell death (pyroptosis). Excessive activation of inflammasomes is associated with many diseases including Alzheimer's, Parkinson's, atherosclerosis, liver disease, and asthma. It is therefore critical to understand how inflammasomes are regulated in human immune cells in order to develop new therapies for inflammatory diseases. In humans (but not mice) several caspase recruitment domain (CARD)-only proteins (COPs) such as CARD16 have been identified as potential inflammasome regulators. This project will investigate the function of CARD16 in human macrophages and will examine how CARD16 interacts with components of the inflammasome such as apoptosis-associated speck-like protein containing a CARD (ASC) and caspase-1. The student will learn a range of techniques and skills such as cell culture, flow cytometry, Western blotting, immunocytochemistry, and microscopy.	YES	https://pure.qub.ac.uk/en/persons/rebecca-coll
P06	Dr Eleni Beli e.beli@qub.ac.uk	Retina pathways involved in the altered circadian entrainment of diabetic mice	The student will investigate the impairment of the retina pathways in circadian entrainment in diabetes. The project includes the staining of retina's neurons to identify the cells that are activated in response to light impulses in the retina in health and diabetes. The student will learn dissection, immunofluorescence and microscopy imaging.	YES	https://pure.qub.ac.uk/en/persons/eleni-beli
P07	Dr Beckie Ingram and Dr Rachael Bell b.ingram@qub.ac.uk Rachael.Bell@qub.ac.uk	Cloning novel vaccine candidates to help tackle Anti-Microbial Resistance (AMR)	Bacteria are becoming increasingly resistant to antibiotics; we are approaching a frightening time where we are no longer able to treat infections. The WHO has estimated that without rapid action, by 2050, 10 million people will die annually from AMR infections. The development of vaccines that can prevent these infections and limit our use of antibiotics is essential. Within this project, the student will clone identified potential vaccine candidates and recombinantly express the proteins. They will learn a range of bacterial culture and molecular biology techniques.	YES	https://pure.qub.ac.uk/en/persons/beckie-ingram

P08	Dr Derek Brazil d.brazil@qub.ac.uk	Identifying the mechanisms of Gremlin1 signalling in colorectal cancer	Levels of the secreted BMP antagonist Gremlin1 1 (GREM1) are increased in a range of human diseases including lung fibrosis, diabetic nephropathy and a range of human cancers including colorectal, breast and lung cancer. The canonical model of GREM1 signalling is binding to bone morphogenetic proteins (BMPs) and preventing BMP receptor signalling. However, many reports have identified additional non-BMP signalling modalities for GREM1 that may be significant for the pathogenic role of GREM1 in human disease. This project will examine a recently reported GREM1 signalling pathway involving MEK1/2 and ERK1/2 in colorectal cancer cells. These experiments will help us to shed new light on the pathogenic signalling for GREM1 in human disease. Aims: 1. Validate GREM1 inhibition of BMP signalling in HeLa and HCT116 cells. 2. Establish Western blotting assays for pERK1/2 and pMEK1/2. 3. Treat cells with rhGREM1 over a range of concentrations and time-points and examine pERK1/2 and pMEK1/2 readouts. 4. Measure levels of pERK1/2 and pMEK1/2 in paraffin sections from tumour-bearing cancer mice using immunohistochemistry. Expected Outputs: Validation of novel GREM1 signalling pathways in cancer cells will be an important step in improving our understanding of GREM1 signalling in health and disease.	YES	https://pure.qub.ac.uk/en/persons/derek-brazil
P09	Prof. Miguel A. Valvano m.valvano@qub.ac.uk	Beating the "Last of Us": Cross-kingdom fungal-bacteria interactions	The rise of antibiotic resistance and growing human populations with compromised health and immunity, make bacterial and fungal pathogens a formidable threat to human health. Infections by fungal pathogens are increasingly becoming more prevalent, especially in immunocompromised people; there is an urgent need for novel and effective therapies to curtail these infections. To develop new treatments, we require a deeper understanding on how we can harness cross-kingdom bacteria-fungal interactions in the context of the microbiome to keep fungal pathogenesis at check. This project will investigate interactions of the human gut bacterium Enterobacter cloacae complex (Ecc) and the commensal fungus Candida albicans and related species. Ecc bacteria use Type VI secretion (T6SS) to control polymicrobial communities by secreting anti-bacterial and potentially anti-fungal toxins. The Valvano group has recently characterised the diversity of Enterobacter's T6SS and identified several T6SS protein effectors. The aim of this project is to identify, isolate, and biochemically characterise T6SS effector proteins from Ecc bacteria with anti-Candida activity to define their mechanism of action. Techniques to be learned: Microbial propagation and sterile technique, gene cloning, PCR, deletion mutagenesis, fluorescence microscopy confocal imaging, and general protein biochemical methods (e.g., Western blotting, protein expression).	YES	https://publish.uwo.ca/~mvalvano/
P10	Dr David Courtney david.courtney@qub.ac.uk	Visualisation of host factors associating with influenza virus during infection	Our lab works on elucidating novel host factors hijacked by influenza A virus during infection. Once we have identified potential candidates we have to characterise if they are true interactors. One method we use to confirm that we have identified important host factors for virus replication is immunofluorescence. This allows us to visualise within individual cells interactions between viral proteins and host proteins, identifying when in	YES	www.davidgcourtney.com

			infection this association takes place and importantly where. We are looking for a motivated student to help us with the characterisation of some novel host factors we have identified within the lab. In turn, we will train you in molecular virology techniques, influenza infections, immunofluorescence and confocal microscopy to visualise these interactions.		
P11	Dr Guilherme Costa g.costa@qub.ac.uk	Exploring RNA-protein interactions in blood vessels	The vasculature is comprised by a complex network of blood vessels responsible for the vital distribution of supplies to tissues in the body. Although the vasculature is the first organ to form, continued changes in the demand for supplies induce the formation of new vessels throughout life. These processes are regulated by precise molecular and cellular mechanisms that ensure a functional vasculature. In some disorders, such as cancer and diabetes, the dysregulation of these mechanisms results in dysfunctional vessels with critical consequences for tissue health. This project aims to unveil RNA-protein interactions in cells of the vasculature and understand their roles in the correct formation of new vessels. You will be guided and trained by an enthusiastic team of researchers on cell culture techniques, RNA and protein manipulation, and state-of-the art microscopy. You will also learn about image analysis and statistics, gain presentation skills and participate in exciting scientific meetings.	YES	https://gcosta064.wixsite.com/costa-lab
P12	Prof. Denise Fitzgerald and Dr Jessica White d.fitzgerald@qub.ac.uk j.white@qub.ac.uk	How do T cells help repair the brain?	Multiple sclerosis (MS) is an immune-mediated inflammatory disease of the central nervous system (CNS), characterised by loss of myelin from nerve axons (demyelination). Although myelin regeneration (remyelination) can occur in MS, it often fails, leaving axons vulnerable to degeneration. In patients, this leads to symptoms such as impaired sensory, motor and cognitive functions. There are no approved treatments targeting myelin repair. We discovered that regulatory T cells (Treg) accelerate maturation of myelin-producing oligodendrocytes and myelin repair (Nature Neuroscience, 2017). Treg functions are mostly dependent on MHC-II but we have discovered that Treg can drive oligodendrocyte maturation independent of MHC-II. This project will investigate novel mechanism(s) by which Treg promote oligodendrocyte development and remyelination using experimental models of MS and techniques such as cell culture, immunohistochemistry, fluorescence microscopy and image/statistical/ bioinformatic analysis. This will help us to understand how Treg promote repair and potentially identify novel therapeutic targets for CNS demyelinating diseases.	YES	https://fitzgeraldlab.co.uk https://pure.qub.ac.uk/en/persons/denise-fitzgerald
P13	Prof Judy Bradley and Dr Bronwen Connolly judy.bradley@qub.ac.uk b.connolly@qub.ac.uk	Assessing adherence (Fidelity) to the Intervention in a large Multicentre Trial on Remote Rehabilitation in Critical Care	We are delivering a large Multicentre Trial on Remote Rehabilitation in Critical Care in the UK. The Intervention in this trial is complex and we need to know if we are delivering this to a consistent high quality. This studentship will allow you to be part of the team which assesses quality. You will gain experience of how this process happens in trials. You will also have the opportunity to meet teams running clinical trials and e.g. shadow some of our clinical research staff - a great experience to understand how trials are set up and delivered in Belfast.	NO	https://pure.qub.ac.uk/en/persons/judy-bradley https://pure.qub.ac.uk/en/persons/bronwen-connolly