2023 WWIEM SUMMER RESEARCH PROJECTS

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

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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 Derek Brazil d.brazil@qub.ac.uk	Identifying the molecular mechanisms of GREM1 signalling in human disease	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 prostate 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 LNCaP 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 FFPE sections from WT and villin1-GREM1 transgenic 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
P02	Dr Bianca Plouffe b.plouffe@qub.ac.uk	Investigation of the role of the Formyl Peptide Receptor 2 in diabetic retinopathy	Diabetic retinopathy causes irreversible blindness in diabetic patients. Under normal conditions, retinal Müller glial cells (MGCs) control of the extracellular milieu and retinal blood flow. However, in high glucose environment, MGCs undergo important transcriptional and biosynthetic changes and become a major source of inflammatory and angiogenic factors. The upregulation of formyl peptide receptor 2 (FPR2) by MGCs is potentially involved in these changes. The project aims to find out how FPR2 contributes to the cellular responses associated to diabetic retinopathy. The student in charge of this project will have the unique opportunity to develop important experimental competences and skills (cell culture, transfection, microscopy, cell-based assays) as well as valuable knowledge of cellular signalling highly relevant to initiate a future career in biomedical research. This project is particularly exciting, important and self-rewarding as it may lead to an alternative treatment for patients suffering from diabetic retinopathy.	YES	https://pure.qub.ac.uk/en/persons/bianca-plouffe

P03	Dr Dessi Malinova d.malinova@qub.ac.uk	B cell uptake and release of extracellular vesicles	Extracellular vesicles (EVs) are small membrane-bound particles released from cells, which contain cellular components including RNA and protein. EVs have been extensively studied over the last decade in the context of cancer, tissue regeneration, infection, autoimmunity and others. We are interested in how B cells, the immune cells which produce antibodies targeting infectious agents, produce and take up EVs. We will disrupt regulators of these processes and investigate effects on both normal and malignant B cells. The research will likely involve molecular biology, including CRISPR-mediated gene deletion, cell culture, flow cytometry and imaging, giving the candidate experience in a wide range of techniques used in immunology and cell biology.	YES	https://www.malinovalab.com/
P04	Prof Miguel A. Valvano m.valvano@qub.ac.uk	Exploring mechanisms of resistance to last-resort antibiotics	Despite antibiotics are the greatest success story of modern medicine the steady global increase of infections caused by multidrug antibiotic resistant (AMR) bacteria has become one of the greatest threats to human health. The aim of this project is to investigate the mechanisms of resistance of AMR Enterobacter cloacae complex (ECC) bacteria. ECC species can become resistant to Colistin, a last resort antibiotic, either by horizontal transfer of lipopolysaccharide modifying genes or by expression of heteroresistance in the bacterial population. The aims of the project are: (1) testing the virulence potential of ECC isolates in the Galleria mellonella moth larvae infection model (2) conducting qRT-PCR assays to compare the expression of selective colistin resistance associated genes and potential regulators in pre- and post-infection isolates and (3) comparing lipid A profiles of colistin-sensitive and -resistant isolates by mass spectrometry. The student will join a highly accomplished research team and learn both research techniques and scientific methodology.	YES	https://publish.uwo.ca/~mvalvano/
P05	Dr Yvonne Dombrowski y.dombrowski@qub.ac.uk	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.	YES	https://sites.google.com/view/dombrowskilaboratory/home https://pure.qub.ac.uk/en/persons/yvonne-dombrowski

P06	Dr Guilherme Costa g.costa@qub.ac.uk	Finding new strategies to reduce tumour vessel growth	Tumour angiogenesis, a hallmark of cancer, is a critical determinant of disease progression and malignancy. Expanding solid tumours have the capacity of remodelling local vasculature to maximise contact with capillaries and thus, enhance diffusion of oxygen and nutrients required to respond to their increasing energy demands. Better access to the vasculature also facilitates the dispersion of tumour cells that can reach distant metastatic sites. On the other hand, the new tumour vessels tend to display abnormal features, which limit drug delivery and further potentiate angiogenesis. In this project you will explore the role of particular RNAs in tumour-associated vessels, how they can be manipulated to prevent dysregulated vessel growth and consequently, reduce tumour expansion. You will join a team of researchers to guide you through daily life in the lab, and you will gain skills in cell culture techniques, 3D models of tumour angiogenesis, molecular biology techniques and cutting-edge microscopy.	YES	https://gcosta064.wixsite.com/costa-lab
P07	Dr Bettina Schock b.schock@qub.ac.uk	The effect of DREAM on collagen production and deposition from lung fibroblasts	Fibroblast transition into myofibroblasts contributes to the development of pulmonary fibrosis (PF). Incidences of PF are rising in the UK and worldwide, but there are limited treatment options. The factors contributing to the development of PF are still unclear, but pulmonary hypoxia enhances the deposition of extracellular matrix by fibroblasts. Work so far suggests that hypoxia induced HE4 in airway epithelial cells, plays a key role in collagen production from lung fibroblasts. HE4 also induces the inflammatory regulator DREAM. In this project you will investigate if overexpression of DREAM in lung fibroblasts contributes to enhanced collagen deposition. If so, DREAM may become a novel target for anti-fibrotic drugs. Techniques you will learn include sterile working, cell culture of human lung fibroblasts, protein overexpression, analyses of HE4 (ELISA), DREAM (Western Blotting, qRT-PCR) and collagen (Western Blotting, Sirus Red staining). Additionally, you will become proficient in presentations and teamwork.	YES	https://pure.qub.ac.uk/en/persons/bettina-schock
P08	Dr Rebecca Coll r.coll@qub.ac.uk	Examining mechanisms of ferritin-mediated inflammation in the context of acute respiratory distress syndrome	ARDS is an acute respiratory disease defined by immune mediated breakdown of the alveolar-capillary barrier which has a high mortality rate (30-40%). Recent work has shown that ferritin, an iron storage molecule, is significantly elevated in some ARDS patients and that it is associated with inflammasome signalling. Inflammasomes are intracellular protein complexes that sense danger- and pathogen-associated molecular patterns and trigger a highly inflammatory innate immune response. This NLRP1 inflammasome which has recently emerged as a key inflammasome sensor in the respiratory epithelium and may contribute to damaging inflammation seen in ARDS. This project will examine whether ferritin can prime the NLRP1 inflammasome in myeloid and epithelial cells, potentially revealing a new target for anti-inflammatory therapies in ARDS. The student will learn techniques including cell culture, cell death assays, Western blotting, ELISA, immunocytochemistry, and qRT-PCR.	YES	https://pure.qub.ac.uk/en/persons/rebecca-coll

P09	Northern Ireland Clinical Research Facility - Prof Judy Bradley/Roisin Martin NICRF@qub.ac.uk	Northern Ireland Clinical Research Facility NICRF (2 Placements available)	This student will gain experience of working within the NI clinical research ecosystem. They will work within a multidisciplinary team and contribute to one or more ongoing projects. These projects will involve laboratory work (collection, processing of biological samples); analyzing of data collected within clinical trials; analysis of SOPs/guidance documents within the NICRF; reviewing working processes within the NICRF; exploring how to optimize patient and public engagement in the NICRF. They will gain a wide range of experiences including exposure to clinical trial activity, project management skills, analyzing datasets and preparing papers and communication and exposure with multiple stakeholders (including researchers, clinicians, patients and patient and public involvement.	YES	https://www.qub.ac.uk/research-centres/TheWellcomeTrust-WolfsonNorthernIrelandClinicalResearchFacility/
P10	Prof David Simpson and Dr Evan Troendle david.simpson@qub.ac.uk	Uncovering Mitochondrial Haplotypes in Diabetes: A Bioinformatic Study on Lineage Tracing during Cell Development	Recent studies have hinted at a crucial role played by mitochondria in the development of diabetes, however, further research is required to fully understand the impact of mitochondrial genetics on the disease. This research project aims to understand the role of mitochondrial DNA (mtDNA) in the development of diabetes. We will use computational bioinformatic techniques to discover mitochondrial haplotypes in diabetes for lineage tracing during cell development. The project will involve analyzing single-cell sequencing data to compare the genetic signatures of cells from healthy and diabetic mouse models, with a focus on identifying variations in mtDNA between these groups. This will enable us to understand the role of mtDNA in the development of diabetes at the cellular level. This project will provide hands-on experience in bioinformatic and scientific computing techniques and will be an excellent opportunity for students interested in diabetes research and computational biology.	NO	https://pure.qub.ac.uk/en/persons/evan-troendle https://pure.qub.ac.uk/en/persons/david-simpson
P11	Dr Bronwen Connolly b.connolly@qub.ac.uk	Measuring the metrics of outcome reporting in trials of physical rehabilitation in critical illness	Systematic review examining reporting of recommended data items for outcomes used for evaluation in clinical trials of physical rehabilitation in critical illness. Specifically, examining adherence to SPIRIT guidance (Standard Protocol Items: Recommendations for Interventional Trials, https://doi.org/10.7326/0003-4819-158-3-201302050-00583) that outcomes reported in clinical trials should include detail of i) measurement variable, ii) participant-level analysis metric, iii) method of aggregation, and iv) measurement time-point. The student will have the opportunity to work within an internationally renowned, experienced, multi-professional research group, and gain exposure and awareness to a wide range of current clinical trials. Key skills acquired will include: i) experience of systematic review processes for database searching, screening, and selecting eligible evidence, ii) knowledge of outcome reporting and its importance within the design of clinical trials, iii) experience in data extraction, iv) application of a range of quantitative and qualitative techniques to appropriately analyse and synthesise relevant data.	NO	https://pure.qub.ac.uk/en/persons/bronwen-connolly

P12	Dr Bronwen Connolly and Professor Bronagh Blackwood b.connolly@qub.ac.uk	Physical rehabilitation for recovery from critical illness - a Cochrane systematic review	Skeletal muscle wasting and weakness are complications of critical illness that contribute to physical and functional impairments in intensive care unit (ICU) survivors. Impairments may persist for many years and can markedly influence health-related quality of life. Rehabilitation is a key strategy in recovery of patients after critical illness. Physical rehabilitation interventions target muscle wasting and weakness and can be delivered whilst patients are in the ICU as well as following discharge. This systematic review will evaluate the effectiveness of these interventions for improving patient outcomes. The student will work within an internationally renowned, experienced, multi-professional research group, and gain exposure and awareness to a wide range of clinical trials. Key skills acquired will include: i) experience of systematic review processes for database searching, screening, and selecting eligible evidence, ii) experience in data extraction specifically related to physical rehabilitation trials and selected outcomes, iii) application of appropriate techniques to synthesise relevant data.	NO	https://pure.qub.ac.uk/en/persons/bronwen-connolly
P13	Professor Bronagh Blackwood b.blackwood@qub.ac.uk	Preventing delirium in children in intensive care	You will have the opportunity to work within a multidisciplinary research group examining ways of preventing the occurence of paediatric delirium in the ICU. This project will involve (1) identifying available research studies that have tested non-pharmacological methods; (2) determining the quality of the clinical studies; and (3) extracting relevant detail on the methods used and outcome data on their effectiveness. You will receive training in these skills that you can put into practice. Ultimately, you will achieve the experience of being an active systematic review team member that will determine the best evidence-based approach to preventing delirium in critically ill children. You will also be a co-author on the subsequent publication. To undertake this project you will require knowledge and skills in searching electronic databases (such as Medline, PubMed). You will also require good attention to detail and ability to keep full, clear and accurate records.	NO	https://pure.qub.ac.uk/en/persons/bronagh-blackwood
P14	Professor Bronagh Blackwood b.blackwood@qub.ac.uk	Determining how to detect sedation and opiate withdrawal in critically ill patients	You will have the opportunity to work with a multidisciplinary research group examining ways of screening critically ill patients for signs of withdrawal in the ICU. This project involves (1) identifying available research studies that developed and tested screening instruments; (2) determining the quality of the study methods; and (3) extracting detail on the screening instruments used and their effectiveness. You will receive training in these skills that you can put into practice. Ultimately, you will achieve the experience of being an active systematic review team member that will determine the best evidence-based approach to screen critically ill patients for signs of withdrawal. You will also be a co-author on the subsequent publication. To undertake this project you will require knowledge and skills in searching electronic databases (such	NO	https://pure.qub.ac.uk/en/persons/bronagh-blackwood

			as Medline, PubMed). You will also require good attention to detail and ability to keep full, clear and accurate records.		