2020 WWIEM SUMMER RESEARCH PROJECTS

(subject to funding)

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

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Program Coordinator: Dr Effie Kostareli

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

PROJECT CODE*	SUPERVISOR	TITLE OF PROJECT	PROJECT DESCRIPTION	LB**	RESEARCH GROUP WEBSITE
P2020.01.VT	Dr. Vijay Tiwari V.Tiwari@qub.ac.uk	Deciphering the epigenetic code of neurogenesis	The research in Tiwari lab is aimed at achieving an integrated molecular and systems-level understanding of the mechanisms by which epigenetic machinery and transcription factors contribute to transcriptional reprogramming that defines cell-type identity during brain development and how this communication is altered in diseases such as cancer. To investigate these questions, we employ a multidisciplinary approach combining cutting-edge epigenetics and genomics together with computational biology tools in sophisticated and defined models of neurogenesis and metastasis. The student will learn how to culture cells, perform chromatin assays, qPCR experiments and interact with large scale genomics datasets through bioinformatics tools.	YES	https://pure.qub.ac.uk/en/persons/vijay-tiwari www.tiwarilab.com
P2020.02.DG	Prof David Grieve d.grieve@qub.ac.uk	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.	YES	https://pure.qub.ac.uk/en/persons/david-grieve
P2020.03.TC	Prof Tim Curtis t.curtis@qub.ac.uk	Development of an early stage treatment for diabetic retinopathy.	The prospective student will contribute to a project recently funded by Diabetes UK. We have identified a new drug called 2-HDP that we believe could be effective for the early stage treatment of diabetic retinopathy with significant advantages over current treatment approaches. The goal of this summer studentship is to perform pre-clinical studies to assess the suitability of 2-HDP for the treatment of diabetic retinopathy. The student will take part in this project by learning to do histological work and helping to characterise the neuroprotective effects of 2-HDP in the diabetic retina. Through this lab-based project, the student will gain insight into diabetes research and attain a better understanding of eye anatomy, immunohistochemistry as well as the strength and limits of rodent 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 and confocal laser scanning microscopy.	YES	http://go.qub.ac.uk/tcurtis

P2020.04.MC	Dr Mei Chen m.chen@qub.ac.uk	How ageing changes our eye?	Ageing is a nature process and all parts of our bodies are affected. Age-related retinal degeneration includes conditions such as age-related macular degeneration (AMD), diabetic retinopathy, glaucoma etc. The vertebrate retina has ten distinct layers, the types of cells and their functions in each layer differ. We would like to understand how retinal cells change with ageing. Single cell sequencing technique allows us to know which genes are expressed in which cells. By comparing gene/protein profiles in individual cells from young and aged retina, we are able to know how ageing put its stamp on individual cells. In this summer studentship, we wish to identify a few genes or proteins varying significantly in young and aged retina using various lab techniques including tissue processing (fixation and sectioning), immunohistochemistry /immunofluorescent staining, microscopy /imaging analysis and RT-PCR. The student also has the opportunity to attend and present research findings in group meetings	YES	https://pure.qub.ac.uk/en/persons/mei-chen
P2020.05.CT	Frof.Cliff Taggart c.taggart@qub.ac.uk	Characterization of Rhinovirus- induced airway epithelial cell cytopathogenesis in severe COPD	Chronic obstructive pulmonary disease (COPD) is a common chronic lung syndrome affecting 10% of the global population. Human rhinovirus (HRV) infection is a leading cause of acute exacerbations in COPD but little is known about the relative consequence of HRV interaction with airway epithelial cells in COPD pathogenesis. To address this, we have infected well-differentiated primary bronchial epithelial cell (PBEC) cultures derived from severe COPD patients and healthy matched controls with HRV. We have observed a significantly increased cytopathic effect, apical cell sloughing and apoptosis in HRV infected COPD PBEC cultures compared to infected control PBEC cultures and now wish to learn more about these altered effects in HRV-infected COPD PBECs. The successful student will acquire skills in primary cell culture, quantitative PCR and Western blotting and will contribute important data, which will help delineate the underlying causes of increased cell death in COPD PBECs.	YES	https://pure.qub.ac.uk/en/persons/cliff-taggart
P2020.06.FL	Dr Fionnuala Lundy & PhD student Orla Dunne f.lundy@qub.ac.uk	An investigation into TRPV2 expression in primary bronchial epithelial cells	Our research group is focused on chronic cough in Chronic Obstructive Pulmonary Disease (COPD). The TRP superfamily of ion channels are present in many cell types throughout the body and act as cellular sensors that respond to various stimuli. We have shown that TRPV2, a mechanosensitive ion channel, is expressed in primary bronchial epithelial cells obtained from individuals undergoing bronchoscopy. The aim of this project is to assess if TRPV2 expression differs between non- obstructive and COPD bronchial epithelial cells and also to investigate if TRPV2 localisation differs between mechanically stressed and non-stressed bronchial epithelial cells. Student outcomes include improved project management skills and gaining experience in how to design experiments and analyse results. The student should expect to become competent in a number of lab techniques including protein quantification assays, western blotting, immunostaining and the use of microscopes.	YES	https://pure.gub.ac.uk/en/persons/fionnuala-lundy

P2020.07.BS	Dr Bettina Schock & Amal ElBanna b.schock@qub.ac.uk	Anti-inflammatory itaconate CF airways inflammation	 People with cystic fibrosis (PWCF) suffer from persistent airways inflammation, which activates the Krebs-Cycle. Itaconate (produced through immune responsive gene 1 (IRG1)) is a Krebs-Cycle-derived anti-inflammatory metabolite, inhibiting mitochondrial respiration and inflammatory cytokines (Lampropoulou 2016), but expression and function of itaconate in CF airways are not known. Preliminary data suggest that CF airway cells express little IRG1, however, macrophages express high levels and secreted itaconate (Strelko 2011). We hypothesise that macrophage-derived itaconate will be anti-inflammatory on LPS-stimulated airway epithelial cells. By analysing the expression of itaconate response genes (KEAP1, Nrf2, A20, Mills 2018), we will investigate if the response differs between CF and non-CF cells. You will be using sterile cell culture techniques, mRNA and a colorimetric enzymatic assay. Using an established model of monocyte-derived macrophages, you will determine levels of itaconate, IRG1 and succinate in CF compared to non-CF cells and determine the effect of 4-octyl-itaconate on epithelial cells. 	YES	https://pure.qub.ac.uk/en/persons/bettina-schock/
P2020.08.YD	Dr Yvonne Dombrowski y.dombrowski@qub.ac.uk	Investigating the role of inflammatory processes in early and progressive Multiple Sclerosis	Multiple Sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system (CNS). This project aims to further investigate the role of immune cells in early and progressive MS. The student will study how different types of immune cells influence the composition of immune cell clusters within the brain linings (meninges). These immune cell clusters have been shown to be involved in patients who have more severe MS and develop progressive forms (Bevan et al. Ann Neurol 2018). This work will lead to a better understanding of the roles of immune cells in different stages of MS and potentially lead to further studies seeking to identify novel therapeutic targets or biomarkers. The student will gain experience in immunohistochemistry, brightfield microscopy, fluorescence microscopy, image analysis and statistical analysis.	YES	https://pure.qub.ac.uk/en/persons/yvonne-dombrowski
P2020.09.LG	Prof Lorcan McGarvey, Dr Fionnuala Lundy & PhD student Nicola Roe Lmcgarvey@qub.ac.uk	Investigation of TRPA1 protein expression in COPD vs healthy primary bronchial epithelial cells	Chronic obstructive pulmonary disease (COPD) affects about 3 million people in the UK alone. TRPA1 is a calcium permeable cation channel that has been implicated in the pathogenesis of COPD. Many components of cigarette smoke and pollutants responsible for the pathobiology of COPD are also potent TRPA1 agonists. This project aims to evaluate TRPA1 protein expression in healthy vs COPD primary bronchial epithelial cells. Over the course of the project, the student will investigate and compare protein expression of TRPA1 using immunocytochemistry in both healthy and COPD primary epithelial cells. The student will gain competency in microscopic imaging of stained samples and will learn to interpret, analyse and quantify results using ImageJ software.	YES	https://pure.qub.ac.uk/en/persons/lorcan-mcgarvey

P2020.10.JB	Frof Judy Bradley judy.bradley@qub.ac.uk & Dr Katherine O'Neill & Dr Rebecca McLeese	Assessing the quality of Lung Clearance Index data in healthy adults.	Lung clearance index (LCI) is an emerging outcome measure increasingly used in respiratory clinical trials. As it is a new measure, age matched normative reference data is essential to interpret disease data. In both healthy and disease data, appropriate quality control measures are essential, including assessment of tidal volume variability, repeatability of functional residual capacity (FRC) and time duration of trials. The research team have a project ongoing involving the collection of normative LCI data in healthy individuals aged 18-80 to facilitate the interpretation of LCI in respiratory clinical trials. A significant amount of data has been collected and is available for analysis. The student will become familiar with LCI, a novel lung function measurement and be exposed to research visits in the NICRF. The student will gain experience of how data is collected in clinical trials and will use a range of statistical techniques to summarise relevant data.	ΝΟ	https://pure.qub.ac.uk/en/persons/judy-bradley
P2020.11.AM	Dr Aurelie Mousnier A.Mousnier@qub.ac.uk	Interactions between rhinoviruses and their host cells	Rhinovirus infections are the main cause of the common cold and a major cause of exacerbation of chronic respiratory diseases such as asthma, chronic obstructive pulmonary disease (COPD) or cystic fibrosis, leading to an acute worsening of symptoms. However, there is currently no vaccine or antiviral treatment against rhinoviruses. The student will join the research team of Dr Aurelie Mousnier (2 PhD students, 1 Master student, 1 technician) and will take part in a programme of research to understand how rhinoviruses interact with host cells to replicate. The student will use a range of virology and molecular and cell biology techniques to identify host cell proteins essential for rhinovirus replication. This is expected to lead to the identification of new host targets for the development of antiviral drugs. The student will closely work with a PhD student and will take part in the diverse activities of the group.	YES	https://pure.qub.ac.uk/en/persons/aurelie-mousnier
P2020.12.YG	Yvonne Dombrowski & Guillermo Lopez Campos y.dombrowski@qub.ac.uk g.lopezcampos@qub.ac.uk	Analysis of BPA exposure in mouse	Bisphenol A (BPA) is a plasticiser that is frequently present in common consumer goods such as plastic bottles or containers. BPA is as well an environmental endocrine disrupting compound that is able to affect a large number of biological processes Over the last decade there has been an increased attention over the effects of BPA in human health and its effects in animal models. In this project we will develop and integrative research approach that will combine computational and wet-lab techniques and methodologies. Computational techniques will explore the potential role and impact of BPA in mouse biological pathways, and particularly in the inflammasome. Wet lab techniques will be applied to analyse the presence of detectable levels of BPA in urine of mouse models and comparing the effects of BPA exposure in transgenic animals versus wild type.	YES	https://pure.qub.ac.uk/en/persons/yvonne-dombrowski https://pure.qub.ac.uk/en/persons/guillermo-lopez-campos

P2020.13.RC	Rebecca Coll r.coll@qub.ac.uk	Examining Familial-cold autoinflammatory syndrome- associated NLRP3 mutations in an in vitro cell model	Mutations in the pattern recognition receptor NLRP3 cause an inherited auto-inflammatory disease called Familial-cold autoinflammatory syndrome (FCAS). Individuals with FCAS get cold- induced symptoms such as urticarial rash and fever. The aim of the project is to recapitulate the NLRP3 inflammasome with FCAS mutations in HEK293 cells. Whether cold temperatures affect the activation of the inflammasome will be tested. The student will gain both molecular biology and cell culture skills during this project as well as general experience in working in an innate immunity lab.	YES	https://pure.qub.ac.uk/en/persons/rebecca-coll
P2020.14.C W	آلان المعالي Dr. Chris Watson chirs.watson@qub.ac. uk	Repurposing of Colchicine as a treatment for Heart Failure	Colchicine is a well-established pharmaceutical agent with known anti-inflammatory actions. It exerts its action not through the classical anti-inflammatory pathway involving arachidonic acid but by preventing microtubule polymerisation and thereby stabilisation of inflammatory cells. Widely prescribed for gout, there is growing evidence for its use in several cardiovascular disease conditions associated with inflammation such as pericarditis and atrial fibrillation occurring post coronary artery bypass surgery and pulmonary vein isolation. We are currently studying the use of colchicine in the context of heart failure (heart failure with preserved ejection fraction, HFpEF). Student will investigate the anti- fibrotic and anti-inflammatory impact of colchicine in vitro on cardiac fibroblasts and inflammatory cells and will gain experience in laboratory techniques such as cell culture, qPCR, Western Blot, ELISA.	YES	https://pure.qub.ac.uk/en/persons/chris- watson
P2020.15.JB	Frof Jose Bengoechea j.bengoechea@qub.ac.uk	Klebsiella immune evasion: 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.	YES	https://pure.qub.ac.uk/en/persons/jose- bengoechea

P2020.16.IL	Final State Dr Imre Lengyel i.lengyel@qub.ac.uk	Vascular remodeling in Alzheimer's disease	Alzheimer's disease (AD) is a huge cost to society and even a small improvement in the quality of a patient's life would have enormous benefit for the individuals and their care providers. As AD is becoming an epidemic we need a step-change how we plan future intervention trials for sufferers of dementia. It is often quoted the "eye is a window to the brain" and as such there are several investigations using eye imaging to monitor development and progression of dementia. Based on our recent clinical imaging studies on patients with AD and other types of dementias we found significant changes at the central and peripheral retinal vasculature. The molecular and cellular background for these changes is, however, not yet understood. In this project, we plan to investigate the role of different cell types in vascular remodeling and hope to identify the molecular pathways involved in these changes.	YES	https://pure.qub.ac.uk/en/persons/imre- lengyel
P2020.17.IL	Dr Imre Lengyel i.lengyel@qub.ac.uk	Imaging and image processing in multiple sclerosis in the eye	Multiple sclerosis (MS) has a higher prevalence in Nordic countries and developing better progression monitoring is key to help the MS population. We propose that imaging the eye could provide a good tool to monitor disease progression. Recently we started a feasibility study on MS patients, for which ethics approval is now in place, to conduct this research and the studentship will help with analysing the information collected. The student will also be involved in further data collection but the main emphasis will be to learn and then conduct the analysis of existing images from a variety of imaging modalities like, optical coherence tomography, fundus and ultrawide-field and adaptive optics images.	NO	<u>https://pure.qub.ac.uk/en/persons/imre- lengyel</u>
P2020.18.D M	Dr Dessi Malinova d.malinova@qub.ac.uk	B cell polarity and antigen endocytosis	We have recently identified Endophilin as a regulator of clathrin-independent antigen endocytosis in B cells. This protein has been shown to specifically localise to the leading edge of adherent cells and it has been suggested it may interact with cell polarity regulators during angiogenesis. The process is relatively uncharacterised in B cells and we would like to understand how cell polarity regulators and organelles are organised during B cell antigen uptake in the presence or absence of endophilin. 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://pure.qub.ac.uk/en/persons/dessi- malinova

P2020.19.UP	Frof.Ultan Power u.power@qub.ac.uk	Characterization of novel vaccines	We are generating novel vaccines against bovine respiratory syncytial virus (bRSV) and Nipah virus (NiV) using Sendai virus (SeV) as the vaccine vector. bRSV is a major respiratory pathogen of young calves and causes substantial economic losses worldwide. NiV is an emerging virus with a high rate of mortality in humans and is now endemic in Bangladesh. It is transmitted from fruit bats, while pigs are intermediate hosts. This project will involve the characterization of these novel vaccines in vitro to ensure that the vaccine antigens encoded by the SeV vectors are expressed correctly prior to vaccine trials in calves and pigs, respectively. The project will provide the student with an excellent opportunity to learn about the design and characterization of novel vaccines against major viral pathogens.	YES	https://pure.qub.ac.uk/en/persons/ult an-power