Centre for Cancer Research and Cell Biology

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Investigating the role of the MAPK pathway in mediating resistance to radiation/hormone therapy in prostate cancer.**			
Supervisor(s)	1.Richard Kennedy 2. Nuala McCabe			
School / Centre	CCRCB			
Principal Supervisor's Contact Details	Email: r.kennedy@qub.ac.uk		Tel:	
Degree Pathway for which project is suitable (✓)	Medical Science	x		
	Biochemistry			
	Microbiology			
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation		*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	Prostate cancer (PCa) is the most commonly diagnosed cancer in men in the UK. The current standard of care for stage III/IV prostate cancer patients is radiation and androgen depravation therapy; however resistance to these therapies represents a major barrier for the treatment of PCa. This study aims to identify mechanisms involved in the development of radiation resistance and resistance to enzalutamide, a potent inhibitor of androgen receptor signaling, approved for the treatment of castrate resistant prostate cancer in 2012. We have identified a molecular subgroup in prostate cancer which is driven by MAPK signalling and represents 30% of primary prostate cancers and of 50% metastatic prostate cancers. The MAPK pathway is implicated in a number of roles involved in prostate cancer progression including proliferation, migration and drug resistance. We aim to investigate the role of the MAPK pathway in the development of radiation and enzalutamide resistance using a panel of in house generated radiation and enzalutamide resistant PCa cell lines. We aim to investigate differences in MAPK signaling and markers of epithelial mesenchymal transition (EMT) between parental and resistant cell lines. Furthermore we aim to investigate differences in sensitivity between parental and radiation/enzalutamide resistant cell lines to MAPK inhibition (Trametinib) and inhibitors of EMT (R428, Cabozantinib). Finally we will investigate if MAPK/EMT inhibition resensitises radiation/enzalutamide resistant cell lines to treatment.			
Aims / objectives	1. Investigate MAPK signalling and markers of EMT in radiation/enzalutamide resistant cell lines v parental cells. 2. Investigate the sensitivity of radiation/enzalutamide resistant cell lines to inhibitors of MAPK and EMT signalling. 3. Investigate the efficacy of MAPK/EMT inhibitors in combination with radiation/enzalutamide treatment. Do these agents resensitise resistant cell lines to treatment?			
Techniques employed:	Western blot; Quantitative PCR; cell culture; drug sensitivity assays, radiation sensitivity assays; proliferation assays; migration assays; invasion assays.			

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Optimising immune checkpoint therapy in ovarian cancer**			
Supervisor(s)	1. Richard Kennedy 2. Eileen Parkes			
School / Centre	CCRCB			
Principal Supervisor's Contact Details	Email: r.kennedy@qub.ac.uk		Tel: 028 9097 2443	
Degree Pathway for which project is suitable (✓)	Medical Science			
	Biochemistry	x		
	Microbiology			
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation		*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	Immune checkpoint-targeted therapy (IO) has resulted in limited clinical responses in trials in ovarian cancer. A key research priority is now optimising response to these agents in the clinic. Activation of the cGAS-STING innate immune pathway has been identified as synergistic with anti-PD-1 therapy, and also a means of overcoming resistance to IO. We have reported activation of the cGAS-STING immune pathway as a result of cytosolic DNA released in response to intrinsic and extrinsic DNA damage, and that upregulation of PD-L1 in response to DNA damage is dependent on STING. Therefore, activating the STING pathway as a combination treatment with IO could result in improved clinical responses. We will screen 786 FDA-approved compounds, which can quickly move into the clinic, for activation of PD-L1 expression in ovarian cancer cells. Identified drugs will then be validated for STING activation and activation of immune checkpoints using primary ovarian cancer cell lines, an accurate model of tumour behaviour established from ovarian cancer-associated ascitic fluid in our laboratory. These compounds will be studied in combination with IO using the ID8*Trp53*$^{-/-}$*Brca2*$^{-/-}$ syngeneic mouse model. In addition, compound toxicity will assessed using the normal fallopian tube cell line FT190. Moreover, using ascitic fluid containing tumour and immune cells from patients with ovarian cancer, we will model combination therapy using identified compounds and IO to assess tumour response, and activation of immune response. The ideal treatment combination selected			

	using these methods will be that with the least toxicity and greatest improvement in tumour response to IO.
Aims / objectives	**(1)** Identify drugs which activate the cGAS-STING innate immune pathway and subsequent PD-L1 gene expression **(2)** Validate identified hits in established and novel primary HGSOC cell lines by confirmation of cGAS-STING-PDL1 immune pathway activation.
Techniques employed:	Cell Culture qPCR Western blot In cell western High throughput screen Flow cytometry

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Identification of Targetable Mediators of Drug Resistance in Oesophageal Adenocarcinoma (OAC)**			
Supervisor(s)	1. Richard Turkington 2. Richard Kennedy			
School / Centre				
Principal Supervisor's Contact Details	Email: r.turkington@qub.ac.uk		Tel: 02890 972756	
Degree Pathway for which project is suitable (✓)	Medical Science Biochemistry Microbiology	✓ ✓ 		
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation		*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	Five-year survival rates for oesophageal adenocarcinoma (OAC) remain poor at 15% and treatment strategies for Her2-negative tumours have not changed over the past two decades. The development of drug resistance limits the effectiveness of current chemotherapeutic agents used to treat OAC and the discovery of underlying mechanisms of resistance and novel agents to target these pathways is a priority. We aim to identify pathways of cisplatin resistance through the development and analysis of suitable in vitro models and pre-chemotherapy biopsies. Unravelling the mechanisms of primary resistance will allow ineffective chemotherapy to be avoided in early stage OAC and will also inform the development of rational combinations of therapeutics.			
Aims / objectives	Aim 1: Validation of Genes associated with Resistance to Chemotherapy in OAC To identify pathways and genes associated with resistance to chemotherapy in early stage OAC we have employed a systems biology approach. We have performed transcriptional profiling of 273 formalin fixed paraffin embedded pre-treatment endoscopic OAC biopsies using the Almac Diagnostics Xcel™ array. All OAC patients were treated with cisplatin-based neo-adjuvant chemotherapy followed by surgical resection between 2003 and 2014 at four UK centres. Following normalisation and filtering of the microarray data, pathway and functional enrichment analysis was applied to the resultant gene-set to determine clusters of significantly enriched pathways and Gene Ontology processes. Functional enrichment analysis was performed using Gene Set Enrichment Analysis (GSEA) on the differentially expressed gene lists. We hypothesize that pathways differentially regulated in relation to			

	pathological response may be strong determinants of drug resistance in early stage OAC and so will be particularly relevant. Genes related to the pathways of resistance are currently being assessed by focused siRNA (siRNA, Sigma) screen. We have selected an *in vitro* model representative of chemo-resistance in OAC by aligning transcriptional data according to published methods and those developed by Dr Jaine Blayney (Department of Bioinformatics,Queen's University Belfast). Candidate genes have been selected based on their fold change, biological importance in OAC and potential to be targeted. A focused screen of 84 genes will be performed in triplicate in Q1 2018 to study the effects on cell viability/cytotoxicity of gene silencing, either alone or in combination with cisplatin/5-FU, to discover targets which are not toxic in their own right but interact synergistically with chemotherapy. We anticipate that this screen will generate a number of promising leads and insights into drug resistance in OAC. The prospective student will select one of the candidates from this primary screen for further validation and development. Aim 2: Discovery and mechanistic analysis of a novel drug target in OAC A potential novel drug target will be validated in a panel of oesophago-gastric cell lines with differing mutational contexts. Mechanistic analysis will be performed to discover their mode of action. We will determine the synergism of siRNA mediated knockdown of the selected target with cisplatin/5-FU in a panel of cell lines using MTT assays, combination index values and annexin V/propidium iodide flow cytometry. Western blotting will be performed for markers of apoptosis, such as PARP and cleaved caspase 3, and caspase activity assays will be carried out. Further examination of the effects of the target inhibition will be examined by Western blotting of relevant proteins, 14 day clonogenic assays and DNA repair assays eg comet assays. Should small molecule inhibitors be available for the selected targets these will also be evaluated for their apoptotic and mechanistic effects. **Aim 3: Development of pre-clinical models representative of Cisplatin resistance in OAC.** Research into OAC is currently being hampered by a lack of *in vitro* cell lines which accurately model patient tumours and recapitulate clinical drug responsiveness. We are currently establishing novel primary cell lines using fresh OAC tissue collected during oesophageal staging and surgery at the Belfast City Hospital. This work will be carried out in collaboration with the OCCAMS consortium and will also include the storage of fresh frozen tissue for future research. Specimens will be transferred directly from the operating theatre to the research laboratory in complete DMEM media on ice, washed three times with 10ml of phosphate buffered saline, dissected into approximately $3mm^3$ pieces with a scalpel and digested with trypsin-EDTA. Undigested segments will be removed by sedimentation and the clear supernatant spun at 600g for 5 minutes. Cell pellets will be cultured in complete DMEM under standard cell culture conditions. Immortalisation will be performed by lentivirus transfection and oncogene activation. Our group has already successfully established primary cell lines in breast and ovarian cancer and has developed

	optimised standard operating procedures for cell line generation. A cell line representative of cisplatin-resistance will then be used as a model to test the targeting of genes identified in Aim2. In this way we will develop models more representative of oesophageal tumours.
Techniques employed:	Cell Culture qPCR Western blot siRNA knockdown Flow cytometry

Centre for Experimental Medicine

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">INVESTIGATING THE INFLUENCE OF OXIDATIVE STRESS ON ENDOTHELIAL PROGENITOR CELL FUNCTION</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Dr David Grieve
2. Dr Karla O'Neill</td></tr>
<tr><td>School / Centre</td><td colspan="4">CEM</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email: d.grieve@qub.ac.uk</td><td colspan="2">Tel: 028 9097 6468</td></tr>
<tr><td rowspan="3">Degree Pathway for which project is suitable (✓)</td><td>Medical Science</td><td>✓</td><td colspan="2" rowspan="3"></td></tr>
<tr><td>Biochemistry</td><td></td></tr>
<tr><td>Microbiology</td><td></td></tr>
<tr><td>Is project of suitable standard / subject for studentship application? (✓)</td><td>General awards

Wolfson Foundation

Jean Shanks Foundation</td><td>

✓

✓</td><td>Subject-specific awards

British Assoc Dermatologists

Digestive Disorders Foundation

Pathological Society

Other ……</td><td></td></tr>
<tr><td>Background information:</td><td colspan="4">Impaired angiogenesis is known to influence the progression of ischaemic cardiovascular disease. Recent attention has focused on the therapeutic potential of endothelial progenitor cells (EPCs), which are mobilised by ischaemia and are important in vascular homeostasis. Our group has characterised a distinct EPC subtype, termed outgrowth endothelial colony-forming cells (ECFCs), with well-defined endothelial progenitor properties which promote new blood vessel formation in both health and disease. Oxidative stress, and specifically NADPH oxidases, are known to play a key role in cardiovascular disease and emerging evidence suggests that they may also regulate EPC function. Interestingly, we have shown that ECFCs are influenced by oxidative stress, display differential gene expression compared to mature endothelial cells, and are modulated by hypoxia which is a characteristic feature of the ischaemic microenvironment.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">This project therefore aims to investigate the specific influence of oxidative stress and NADPH oxidases on in vitro ECFC function. 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 these cells and their clear potential for the treatment of ischaemic cardiovascular disease.</td></tr>
<tr><td>Techniques employed:</td><td colspan="4">In order to characterise the effects of oxidative stress and NADPH oxidases on ECFC function, studies will be undertaken in cultured cells treated with pro-oxidant compounds in the presence or absence of specific inhibitors of candidate pathways or after genetic manipulation. Expression of key signalling genes will be quantified by real-time RT-PCR and/or western blot and in vitro ECFC migration and proliferation assays will be performed to assess functional effects.</td></tr>
</table>

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science

<table>
<tr><td>Project Title</td><td colspan="4">Metformin and Vascular Health in Diabetes</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Dr Reinhold Medina
2. Dr Christina O'Neill (Postdoctoral Fellow)</td></tr>
<tr><td>School / Centre</td><td colspan="4">SMDBS, CEM</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email:
r.medina@qub.ac.uk</td><td colspan="2">Tel: 028 9097 6477</td></tr>
<tr><td rowspan="3">Degree Pathway for which project is suitable (✓)</td><td>Medical Science</td><td>X</td><td colspan="2" rowspan="3"></td></tr>
<tr><td>Biochemistry</td><td></td></tr>
<tr><td>Microbiology</td><td></td></tr>
<tr><td>Is project of suitable standard / subject for studentship application? (✓)</td><td>General awards

Wolfson Foundation

Jean Shanks Foundation</td><td></td><td>Subject-specific awards

British Assoc Dermatologists

Digestive Disorders Foundation

Pathological Society

Other ……</td><td></td></tr>
<tr><td>Background information:</td><td colspan="4">Metformin remains the first line monotherapy for patients with type 2 diabetes. This is supported by extensive recent clinical studies including systematic reviews and meta-analysis (Maruther et al., Ann Intern Med 2016; Palmer et al., JAMA 2016). In fact, a recent cohort study in 469,988 diabetic patients, indicated that metformin use was associated with a significant decrease risk of all-cause mortality (41%), heart failure (30%), and cardiovascular disease (24%) (Hippisley-Cox et al., BMJ 2016). While clinical evidence for the safety and efficacy of metformin are well-defined, the basic mechanisms of action remain not fully understood. It was suggested that the vascular protective effects of metformin were secondary to the anti-hyperglycaemic effect; however, emerging evidence suggests that metformin might have a direct effect on endothelium. This research project will characterise biological effects of metformin on human endothelial cells cultured under diabetic-like conditions. In addition, it will explore potential molecular mechanisms for these effects. This research project will define a molecular role for metformin in endothelial cell function under diabetes-relevant conditions.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">1. To characterise metformin effects on endothelial cell function.

2. To test if metformin reverses endothelial dysfunction induced by diabetes.</td></tr>
<tr><td>Techniques employed:</td><td colspan="4">➢ Human primary cell culture of endothelial cell lines including progenitor cells.
➢ Endothelial Functional Assays such as clonogenic assay, tube formation assay, vascular permeability assay, and migration assay.
➢ Fluorescent microscopy including confocal.
➢ RT-qPCR, Western Blotting, and Flow Cytometry.
➢ Seahorse XF extracellular Flux analyser.</td></tr>
</table>

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science

Project Title	**Modelling organelle expansion during cellular ageing**			
Supervisor(s)	1. Dr Reinhold Medina 2. Dr Jasenka Guduric-Fuchs (Postdoctoral Fellow)			
School / Centre	SMDBS, CEM			
Principal Supervisor's Contact Details	Email: r.medina@qub.ac.uk		Tel: 028 9097 6477	
Degree Pathway for which project is suitable (✓)	Medical Science	X		
	Biochemistry			
	Microbiology			
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation		*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	Normal diploid cells cannot divide forever, as they replicate and age, they reach a state where they cannot divide any longer (Hayflick limit) and are growth-arrested; however, cells remain viable and metabolically active. This process is known as cellular senescence. Senescence is a normal consequence of cellular ageing and protects the cell from the potential risk of malignant transformation due to oncogenic stimuli. This research project will investigate cellular ageing in human endothelial progenitors and focus on changes in organelles such as nuclei, mitochondria, and lysosomes. We will examine amount and size of these 3 different cellular components. Our lab has optimised protocols to study these organelles using microscopy and flow cytometry. Data will be collected and analysed to model changes in organelle content that occur during cellular ageing.			
Aims / objectives	1) To determine how organelles change with cellular ageing. 2) To establish a predictive biology model to attempt to determine cellular age by assessing cellular organelles.			
Techniques employed:	➢ Human primary cell culture of endothelial cell lines including progenitor cells. ➢ Fluorescent microscopy including confocal. ➢ Flow Cytometry. ➢ Computational work.			

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Testing the anti-microbial effect of leukotriene antagonist zafirlukast on Mycobacterium xenopii and Mycobacterium malmoense</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Cecilia O'Kane
2. Danny McAuley</td></tr>
<tr><td>School / Centre</td><td colspan="4">SMDBS Centre for Experimental Medicine</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email:
c.okane@qub.ac.uk</td><td colspan="2">Tel:
02890976384</td></tr>
<tr><td rowspan="3">Degree Pathway for which project is suitable (✓)</td><td>Medical Science</td><td>x</td><td colspan="2" rowspan="3"></td></tr>
<tr><td>Biochemistry</td><td></td></tr>
<tr><td>Microbiology</td><td>x</td></tr>
<tr><td>Is project of suitable standard / subject for studentship application? (✓)</td><td colspan="2">General awards

Wolfson Foundation

Jean Shanks Foundation</td><td colspan="2">Subject-specific awards

British Assoc Dermatologists

Digestive Disorders Foundation

Pathological Society

Other ……</td></tr>
<tr><td>Background information:</td><td colspan="4">There has been an exponential rise in the prevalence of non-tuberculous mycobacteria (NTM) in respiratory sputum isolates over the past 3 decades. These organisms cause frequently intractable infections in patients with pre-existing structural lung disease, particularly COPD and bronchiectasis. Within this group of infections, Mycobacterium malmoense and Mycobacterium xenopii, are associated with high level morbidity and mortality. Treatment to date focuses on 3-4 antibiotics, which are difficult to tolerate, and associated with poor rates of cure. In our lab we have recently found that a drug currently used for treatment of asthma (drug X) has significant anti-microbial activity against other NTM species. This is incredibly exciting as these infections are highly resistant to multiple antibiotics. Drug X is a safe, well-tolerated drug, currently in use in clinical practice. If it has efficacy against M xenopii and M malmoense this could potentially lead to shorter, more effective and more easily tolerated antimicrobial therapy for patients.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">This study will test
1. the ability of drug X at clinically achievable concentrations, to kill M xenopii in the laboratory
2. the ability of drug X at clinically achievable concentrations, to kill M malmoense in the laboratory</td></tr>
<tr><td>Techniques employed:</td><td colspan="4">Bacterial culture
Bacterial viability assays (Bacter-Glo)
Bacterial quantification by spectrophotometry and colony counting
If possible, depending on student's progress, some basic cell culture and infection assays</td></tr>
</table>

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**A20 and DREAM in pulmonary fibrosis**			
Supervisor(s)	1. Dr Bettina C ***Schock*** (QUB, expertise: Inflammation, A20, DREAM) 2. Amal ***ElBanna*** (QUB, Technical support, day-to-day laboratory supervision, expertise: cell culture, mRNA and protein analyses) 3. Prof John ***Varga*** (Feinberg School of Medicine, Director, Northwestern Scleroderma Programme, expertise: scleroderma)			
School / Centre	Centre for Experimental Medicine			
Principal Supervisor's Contact Details	Email: b.schock@qub.ac.uk		Tel: 07828065833	
Degree Pathway for which project is suitable (✓)	Medical Science	√		
	Biochemistry			
	Microbiology			
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation	√ √	*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	Systemic sclerosis (Ssc) is a chronic a multi-organ (systemic) disease characterized by autoimmunity, vascular lesions and progressive fibrosis that affects predominately the skin and the lungs. To date, the disease is associated with a high mortality and there is no approved therapy (1). In Ssc, fibroblasts are responsible for abnormal extracellular matrix accumulation and skin biopsies have been used for gene expression profiling. To mechanistically investigate pro-fibrotic phenotype conversion, cultured fibroblasts are used. An underlying factor of Ssc fibroblasts is their persistent pro-fibrotic activation which is, in part, driven by persistent activation of the TGFβ / WNT pathway after TLR4 stimulation (2). A20 is a potent regulator of fibrotic and inflammatory pathways and in scleroderma this regulation may be compromised leading to chronic pro-fibrotic and pro-inflammatory stimulation. Pharmacological induction of A20 has anti-inflammatory effects (3), but the degree of A20 induction depends on the expression of the A20 repressor DREAM (4). In normal fibroblasts, TGFß induced sustained downregulation of A20, and abrogated its TLR4-dependent induction, while siRNA-mediated knockdown of A20 enhanced the amplitude of fibrotic responses elicited by TGFß. Moreover, adiponectin induced A20 in fibroblasts and reduced fibrotic outcome measures (5). Moreover, findings from our pilot work using publicly available gene arrays (controls n=38, Ssc n=76) are highly promising: A20 mRNA expression in skin biopsies from patients with scleroderma was significantly reduced while the A20 repressor DREAM was significantly increased. Here we wish to investigate the effect of TGFß stimulation of lung fibroblasts on the expression of A20, DREAM, p21 (cell proliferation) and collagen I and III expression.			

	Furthermore, we wish to examine the effect of A20 inducing drugs (e.g. gibberellic acid, myricetin) on proliferation and collagen expression. References: (1) Allanore Y *et al*. Nat Rev Dis Primers. 2015 Apr 23;1:15002; (2) Bhattacharyya S *et al.* Arthritis Research & Therapy 2016;18:216; (3) Reihill JA *et al*. Br J Pharmacol. 2016 Feb;173(4):778-89; (4) Tiruppathi C *et al*. Nat Immunol. 2014 Mar;15(3):239-47; (5) Bhattacharyya S, Varga J. Curr Rheumatol Rep.2015Jan;17(1):474;
Aims / objectives	This project will characterise A20 and DREAM expression in cultured lung fibroblasts (a commonly used model for Ssc lung fibrosis) in response to TGFß. We hypothesis that augmentation of A20 (decreasing DREAM) will reduce proliferation and collagen expression in cultured lung fibrosblasts. Fibroblasts will be grown in submersion, stimulated (TGFβ) and A20, the repressor DREAM (mRNA, protein), proliferation marker p21 and collagen I and III (mRNA) will be determined by qRT-PCR and Western Blotting.
Techniques employed:	Tissue culture and sterile working techniques (culture of human lung fibroblasts, stimulation with TGFß2 (10 ng/ml) in the presence and absence of the predicted drugs), collection of total mRNA, conversion into cDNA and quantitative real time PCR. Protein analyses by Western Blotting. Statistical analyses of results. Transferrable skills: Working in a team and alone, presentation of data and communication to other members the laboratory and the wider scientific community and the collaborators.

Centre for Medical Education

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**How do medical students learn to be 'good' doctors?**			
Supervisor(s)	1. Tim Dornan			
School / Centre	Centre for Medical Education			
Principal Supervisor's Contact Details	Email: timothy.dornan@gmail.com		Tel: 07712 528565	
Degree Pathway for which project is suitable (✓)	Medical Science	x		
	Biochemistry			
	Microbiology			
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation		*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	This intercalation offers one or maximum two highly motivated students the opportunity to work as members of a small, collegial research group, specialising in education research. The distinguishing feature of our work is that it is as much a social science as a medical science. The main strand of our work is research into how medical students learn to practise medicine amidst the social complexity of workplaces. This offers benefit on several quarters. It helps candidates learn to be good doctors; it helps them learn to teach; and it teaches them ways of thinking that are not so strongly promoted by the mainstream medical curriculum. We 'tailor' projects to the wishes and needs of individual students.			
Aims / objectives	Projects we can offer this coming year include: - How do children experience hospitals and how can they contribute to medical students' and doctors' learning? - How do medical students learn to 'hold their own' in hospital settings, and prescribe safely there - How can medical humanities contribute to medical education			
Techniques employed:	We have expertise in a range of methodologies, chiefly qualitative research. This means interviewing or conducting discussions with people in order to learn about social situations, like practising medicine or prescribing. We encourage every candidate to learn how to conduct a rigorous literature review. These may, if done well, lead to publications. We can offer training in survey research, implementation science, and many other research techniques.			

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Interprofessional simulation based education: a scoping review</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Dr Briegeen Girvin
2. Dr Gerry Gormley</td></tr>
<tr><td>School / Centre</td><td colspan="4">1. School of Pharmacy
2. Centre for Medical Education</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email:
b.girvin@qub.a.cuk</td><td colspan="2">Tel:
02890972017</td></tr>
<tr><td rowspan="3">Degree Pathway for which project is suitable (✓)</td><td>Medical Science</td><td></td><td colspan="2" rowspan="3"></td></tr>
<tr><td>Biochemistry</td><td></td></tr>
<tr><td>Microbiology</td><td></td></tr>
<tr><td>Is project of suitable standard / subject for studentship application? (✓)</td><td>General awards

Wolfson Foundation

Jean Shanks Foundation</td><td></td><td>Subject-specific awards

British Assoc Dermatologists

Digestive Disorders Foundation

Pathological Society

Other
……</td><td></td></tr>
<tr><td>Background information:</td><td colspan="4">BACKGROUND
Interprofessional education
The demands of modern healthcare provision are complex and increasingly revolve around teams of professionals, rather than relying on individual practitioners. Competent individuals may not necessary make competent teams. Professional development that focuses on collaborative practice is known to improve the quality of patient care. Such a focus on interprofessional skills must be established at undergraduate level.

Simulation based education
Simulation based Education (SBE) has emerged as a significant educational methodology that can advance student learning and best prepare healthcare professionals for practice. The evidence base is now irrefutable of the benefits that SBE can bring to patient care. The simulated experience provides a realistic and challenging learning opportunity that can prepare healthcare teams to perform successfully in real clinical settings.

The emerging roles of pharmacy
The General Pharmaceutical Council Standards on the initial education and training of pharmacists advise that the MPHARM degree must include practical experience of working with patients, carers and other health care professionals. This is currently</td></tr>
</table>

	achieved through a mix of off-site placement visits, using patients, carers and other health care professionals in-class, and simulations. Qualified pharmacists are increasingly being involved in more clinical roles which involve close interprofessional working both in secondary and primary care. Examples include managing and prescribing for patients with long term conditions, such as hypertension, heart failure, diabetes, asthma and COPD. The expanding roles for pharmacists require competence in various skills such as clinical skills (including physical assessment), critical thinking, communication and team work skills. Pre-2011, most of the published literature around use of simulation in the education of health care professionals has been in medical and nursing schools and less often in pharmacy. Preliminary evidence shows that interprofessional learning through simulation enables participants to practice teamwork and communication skills that are essential for preventing errors and patient harm (Crea, 2011). A review of the published literature on the effectiveness of simulation in pharmacy education and particularly where simulation has been used in interprofessional education, would be a huge benefit to universities when planning training to prepare their students for work in practice.
Aims / objectives	**AIM** • The overall of this project is to establish an understanding of the role of simulation based education in the role of pharmacist training and interprofessional education. **OBJECTIVES** • Undertake a *scoping review* to map current evidence relevant to a SBE in pharmacy and interprofessional education • identify all relevant publications, and draw whatever conclusions the evidence supports in the use of SBE in pharmacy • consider how this information may have an impact on educational policy and practice • Identify topics for future educational research and development.
Techniques employed:	The successful applicant will use a *scoping review* methodology to review the literature. Such a form of literature review is exploratory in nature that aims to map current evidence relevant SBE in pharmacy The review will follow the methodological steps for scoping reviews devised by Arksey and O'Malley (2005) Namely: Step 1: Identifying the research question Step 2: Finding relevant articles Step 3: Selection of relevant articles Step 4: Charting the data Step 5: Collating and summarizing the data

	Step 6: Consultation exercise (focus groups) The proposed benefits to the successful applicant 1) Generate and synthesize knowledge that could be used to influence practice and policy 2) Develop skills in critical thinking, research methods, searching the evidence base, interview skills, presentation skills 3) If would be the hope that this work will lead to a publication in a scientific journal and presentation at academic conferences Arskey H and O'Malley L. Scoping Studies: Towards a Methodological Framework. Int J social Research Methodology 2015; 8 (1): 19-32 Crea KA. Patient simulation. Practice skill development through the use of human patient simulation. American Journal of Pharmaceutical Education 2011; 75 (9): Article 188.

Centre for Public Health

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	Dementia data analytics in Northern Ireland			
Supervisor(s)	1. Dr Bernadette McGuinness 2. Prof Peter Passmore			
School / Centre	CPH			
Principal Supervisor's Contact Details	Email:b.mcguinness@qub.ac.uk		Tel:90978959	
Degree Pathway for which project is suitable (✓)	Medical Science	x		
	Biochemistry			
	Microbiology			
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation		*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	We are funded by Atlantic Philanthropies, OFMDFM and Department of Health to carry out a large dementia analytics project in Northern Ireland. This will include analysis of data from the Data warehouse, GP data and use of the Honest Brooker service. Outputs will include: 1 Yearly reports for professionals, political and administrative decision makers; will inform policy and predictions of cost 2 Framework for ensuring quality of diagnosis, treatment and care across the country and Europe 3 Use to further develop Dementia National Strategy 4 Generate new research hypotheses 5 Link with other European and worldwide registries 6 Publications in international peer-reviewed high impact journals			
Aims / objectives	Several projects will be carried out by the team including the intercalated student. One example is analysis of anticholinergic drug use and mortality in patients with dementia. Hypothesis: Patients with dementia with a high anticholinergic drug burden have an increased mortality rate compared to patients with dementia not on anticholinergic drugs. Methods: Retrospective analysis of GP prescriptions of anticholinergic drugs in patients with dementia compared to patients with dementia not on anticholinergic drugs and mortality rates in both over a five year period.			
Techniques employed:	Statistical analysis of large datasets			

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Microvascular, cognitive and renal outcomes in UK Biobank**			
Supervisor(s)	1. Dr Gareth McKay 2. Dr Bernadette McGuinness 3. Mr Euan Paterson			
School / Centre	Centre for Public Health			
Principal Supervisor's Contact Details	Email: g.j.mckay@qub.ac.uk		Tel: 90978958	
Degree Pathway for which project is suitable (✓)	Medical Science	✓		
	Biochemistry			
	Microbiology			
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation		*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	There is a paucity of evidence relating to primary and secondary prevention of cognitive impairment. The retina is derived from neural tissue and connected to the brain via the optic nerve, sharing cellular similarities to the central nervous system. Retinal blood vessels are amenable to direct non-invasive visualisation and measurement allowing investigation of early microvascular changes prior to the development of conditions of a vascular nature. Renal dysfunction and vascular disease have been reported in association with cognitive outcomes in several cross-sectional and longitudinal studies. Retinal vascular parameters will be evaluated against cognitive and renal function measures from UK Biobank (UKBB). Captured retinal measures will include parameters such as vessel calibre, tortuosity, and branching patterns. A wide range of confounding variables will also be considered. This research will help determine whether retinal microvascular parameters offer additional clinical utility in identifying individuals with reduced cognitive functioning and if renal impairment is a potential confounding factor.			
Aims / objectives	We are receiving data for 6998 participants from UKBB. This study will analyse cross sectional data to evaluate associations between retinal vascular parameters and cognitive and renal function outcomes.			

Techniques employed:	This study will use VAMPIRE (Vascular Assessment and Measurement Platform for Images of the REtina) software to identify and measure retinal microvasculature changes from digital photographs acquired from the UK Biobank. The standardised measured area is defined within the region 0.5-2.0 disc diameters from the optic disc margin. Fractal analysis will quantify geometric branching complexity and density of retinal vessels providing a holistic overview of retinal microvascular health. Statistical analyses will evaluate associations between retinal microvascular variation and cognitive and renal function with consideration of potential confounding variables.

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Dietary patterns and microvascular health – a study of renal dysfunction in the UK Biobank cohort</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Dr Gareth McKay
2. Prof Jayne Woodside
3. Mr Euan Paterson
4. Dr Charlotte Neville</td></tr>
<tr><td>School / Centre</td><td colspan="4"></td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email: g.j.mckay@qub.ac.uk</td><td colspan="2">Tel: 90978958</td></tr>
<tr><td rowspan="3">Degree Pathway for which project is suitable (✓)</td><td>Medical Science</td><td>✓</td><td colspan="2" rowspan="3"></td></tr>
<tr><td>Biochemistry</td><td></td></tr>
<tr><td>Microbiology</td><td></td></tr>
<tr><td>Is project of suitable standard / subject for studentship application? (✓)</td><td>General awards

Wolfson Foundation

Jean Shanks Foundation</td><td></td><td>Subject-specific awards

British Assoc Dermatologists

Digestive Disorders Foundation

Pathological Society

Other ……</td><td></td></tr>
<tr><td>Background information:</td><td colspan="4">The retinal vasculature is accessible to direct and repeated non-invasive assessment enabling detection of early microvascular changes prior to clinically significant events. A good diet is associated with reduced chronic disease risk, but the association between diet and retinal vascular health is underexplored.

Clinical data derived from the UK Biobank will be used to identify individuals with renal impairment (urinary albumin/creatinine ratio (ACR) > 3mg/mmol) for comparison with control individuals with normal ACR. Comparisons will examine retinal vessel measurements, including microvascular parameters such as calibre, tortuosity, and branching patterns. A wide range of confounding variables will be considered in the analysis.

This studentship will analyse dietary data to examine food, whole diet and patterns of intake and explore whether diet is associated with retinal vessel health and renal impairment in this population.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">We are receiving data for 6998 participants from the UKBB. This study will analyse cross sectional data from a subset of these participants to evaluate associations between dietary patterns, microvascular health and renal function.</td></tr>
</table>

Techniques employed:	This study will use VAMPIRE (Vascular Assessment and Measurement Platform for Images of the REtina) software to identify and measure retinal microvasculature changes from digital photographs acquired from the UK Biobank. The standardised measured area is defined within the region 0.5-2.0 disc diameters from the optic disc margin. Fractal analysis will quantify geometric branching complexity and density of retinal vessels providing a holistic overview of retinal microvascular health. Statistical analyses will evaluate potential associations between dietary patterns, microvascular variation and renal function with consideration of potential confounding variables.

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Deep phenotyping and genetic analysis for Behçet's disease – a complex, multifactorial rare disease</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">AJ McKnight</td></tr>
<tr><td>School / Centre</td><td colspan="4">SMDBS – Centre for Public Health</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email: a.j.mcknight@qub.ac.uk</td><td colspan="2">Tel: 02890 638460 (shared line)</td></tr>
<tr><td rowspan="3">Degree Pathway for which project is suitable (✓)</td><td>Medical Science</td><td>Yes</td><td colspan="2" rowspan="3"></td></tr>
<tr><td>Biochemistry</td><td>Yes</td></tr>
<tr><td>Microbiology</td><td>No</td></tr>
<tr><td>Is project of suitable standard / subject for studentship application? (✓)</td><td>General awards

Wolfson Foundation

Jean Shanks Foundation</td><td>Yes

Yes</td><td>Subject-specific awards

British Assoc Dermatologists
Digestive Disorders Foundation
Pathological Society

Other ……</td><td>Yes

Don't know…</td></tr>
<tr><td>Background information:</td><td colspan="4">The European Union (EU) definition of a rare disease is one that affects ≤5 per 10,000 people, with ~30 million persons directly affected in the EU and ~106,000 affected in Northern Ireland. These diseases are individually rare, but collectively common and represent a significant public health problem. This project investigates inherited risk factors and the impact of living with a selected rare disease: Behçet's disease (BD).

Genetic and environmental factors contribute to BD, but the process of diagnosis is challenging with inconsistent clinical manifestations of this disease. A recent survey of individuals living with rare disease(s) in Northern Ireland revealed ~50% of individuals receive ≥1 misdiagnosis with $^{1}/_{20}$ seeing >10 doctors. Individuals with BD report a wide range of symptoms, which are variable in onset, severity, and frequency of flare-ups for this systemic vasculitis. This disease involves abnormal inflammation / immune responses and common features include recurrent ulcers, skin lesions, and serious eye inflammation.

BD is most often reported in populations along the Silk Road. The highest prevalence is reported in Turkey at 20-420/100,000, compared 1.5/100,000 individuals in the UK. Recent mapping through general practitioners revealed a much higher than expected prevalence of 12.6/100,000 in the Northern Ireland population. This higher than expected 'UK' prevalence, and the identification of several families with multiple members diagnosed, makes NI ideal to explore genetic risk factors for BD.</td></tr>
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	This project involves deep phenotyping and strategies to improve recognition of Behçet's disease, identify genetic risk factors, and improve data sharing.
Aims / objectives	The primary aim of this project is to survey patients affected by Behçet's disease, identify genetic risk factors associated with BD in Northern Ireland, and evaluate information sources for patients.
Techniques employed:	This project will involve generating data from online surveys and focus groups, as well as state-of-the-art genotyping (next generation sequencing and / or high density microarrays) to analyse more than one million unique genetic markers for association with Behcet's Disease in a Northern Ireland population. For the dedicated student, this project may also include working with multiple stakeholders and using mixed methodological approaches to evaluate access to appropriate information sources, the social impact of living with this rare disease, and evaluate mental health and wellbeing.

Honours Project for Intercalated BSc Degrees (2018-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Gene-environment interactions in Age-related macular Degeneration**			
Supervisor(s)	Amy Jayne McKnight & Ruth Hogg			
School / Centre	Centre for Public Health			
Principal Supervisor's Contact Details	Email: a.j.mcknight@qub.ac.uk		Tel: (0)28 9097 6359	
Degree Pathway for which project is suitable (✓)	Medical Science	X		
	Biochemistry			
	Microbiology			
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation		*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	Genome-wide association studies have proved successful in revealing a significant proportion of the heritability related to AMD, with the most recent report highlighting 52 independently associated common and rare variants across 34 loci[1], however missing heritability still remains. It is also well established that both genetic and environmental factors contribute to the development of AMD, but how these interact to result in the characteristic phenotypes in AMD is not well understood. There have been to date no large-scale population based studies involving cohorts well-phenotyped for AMD as well as characterised for the many demographic and environment risk factors known to be associated with the disease. The Northern Ireland Cohort for the Longitudinal Study of Aging provides such an opportunity as approximately 4,500 participants have underwent an extensive home interview, dietary assessment and health assessment which include multi-modal retinal imaging. The retinal images (colour, OCT, infra-red, autofluorescence and ultra-wide field Optomap images) have been graded for AMD including novel phenotypes such as reticular pseudodrusen/subretinal drusenoid deposits. This project would seek to relate genome-wide association data with environmental risk factors and presence of various AMD related phenotypes.			
Aims / objectives	To explore the relationship between genetic risk loci and environmental risk factors in AMD through the use of a genome-wide scan in a well-phenotyped population-based study in Northern Ireland (NICOLA Study).			

Techniques employed:	Bioinformatics, multivariate statistical analysis, retinal grading.

Honours Project for Intercalated BSc Degrees (2018-2019)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Improving the food environment in primary schools**			
Supervisor(s)	1. Professor Jayne Woodside 2. Dr Michelle McKinley			
School / Centre	Centre for Public Health			
Principal Supervisor's Contact Details	Email: j.woodside@qub.ac.uk		Tel: 02890978942	
Degree Pathway for which project is suitable (✓)	Medical Science	x		
	Biochemistry	x		
	Microbiology			
Is project of suitable standard / subject for studentship application? (✓)	*General awards* Wolfson Foundation Jean Shanks Foundation		*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	There is growing concern about diet quality in childhood and how poor nutrition may impair brain development and cognitive function, with low quality diets being associated with lower academic achievement. Children, particularly in urban settings, also often have little knowledge of where their food comes from. This project will be based in a wider body of work aiming to investigate the potential impact of engagement with the food sector, and alteration of the food environment in the primary school setting on diet, health and wellbeing outcomes.			
Aims / objectives	1) To determine the effect of changes in the school food environment on diet, health and wellbeing outcomes.			
Techniques employed:	1) Systematic literature review 2) Qualitative research methodology			