Centre for Cancer Research and Cell Biology

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Investigating an association between the DDRD molecular subgroup and expression of immune checkpoint pathway members in breast cancer**			
Supervisor(s)	1. Prof Richard Kennedy 2. Dr Nuala McCabe			
School / Centre	Centre for Cancer Research and Cell Biology (CCRCB)			
Principal Supervisor's Contact Details	Email: r.kennedy@qub.ac.uk		Tel: +44 (0)28 9097 2777	
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:	We have identified a DNA damage response-deficient (DDRD) molecular subtype within breast cancer and demonstrated that this represents loss of the S-phase specific DNA damage response mechanism, the Fanconi Anaemia (FA)/BRCA pathway (Mulligan et al., 2014). A 44-gene assay identifying this subtype was validated as predicting benefit from DNA-damaging chemotherapy. Importantly, upregulation of interferon-related genes is observed within the DDRD molecular subtype (including the chemokines *CXCL10* and *CCL5*, and the immune inhibitory genes *PD-L1* and *IDO1)*. Recently we have shown that activation of the innate immune STING-mediated pathway is responsible for chemokine production in response to DNA damage *in vitro*, resulting in an inflammatory microenvironment in DDRD breast tumours (Parkes et al., 2017). Activation of this pathway and associated upregulation of the immune inhibitory gene, *PD-L1*, may explain the paradoxical lack of T-cell-mediated cytotoxicity observed in DDRD tumours. This provides a rationale for exploration of DDRD in the stratification of patients for immune checkpoint–based therapies. Blockade of immune checkpoints is perhaps the most promising approach to activation of therapeutic anti-tumour immunity. Many of the immune checkpoints are initiated by ligand–receptor interactions at the interface between cancer cells and host immune cells, and as such, they can be readily blocked by antibodies or modulated by recombinant forms of ligands or receptors. Blockade of either PD-1 or its ligands has demonstrated consistent immune-potentiating effects and has been shown to have potent antitumor activity in both murine tumour models and clinical trials including non-small-cell lung cancer, melanoma, and renal-cell cancer. There are currently 6 anti-PD-L1 or PD-1 therapies in clinical trials for cancer (www.clinicaltrials.gov). In addition to the PD-1 pathway,			

	there are dozens of other immune-modulating receptor–ligand interactions that may be targeted clinically.
Aims / objectives	We wish to investigate the expression of additional immune-inhibitory genes (e.g. *CTLA4*, *HVEM*, *LAG3*, *OX40* etc.) for an association with DDRD biology; this could provide a rationale for further exploration of immune checkpoint-modulating therapies within DDRD positive cancers. To fulfil this aim we will perform real-time quantitative PCR (RQ-PCR) assays to analyse the mRNA expression of selected immune checkpoint gene targets within established isogenic cell line models. The BRCA1-mutant MDA-MB-436 cell line stably expressing either an empty vector control or wild type BRCA1 represents an *in vitro* model of DDRD-positivity and –negativity, respectively. To investigate the requirement of the STING pathway and its component proteins for the regulation of immune-inhibitory gene expression we will perform siRNA knockdowns of pathway members (e.g. STING, cGAS, IRF3) in combination with DNA damaging chemotherapy and assess the expression of immune inhibitory gene targets.
Techniques employed:	• Routine cell culture, siRNA transfections, drug treatments • RNA extraction, cDNA synthesis, RQ-PCR and gene expression analysis

Centre for Experimental Medicine

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Investigate novel therapies for Cardiovascular disease and Diabetes using patient specific induced pluripotent stem cells.</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Dr Andriana Margariti

2.</td></tr>
<tr><td>School / Centre</td><td colspan="4">Medicine / CEM</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email: Email:
a.margariti@qub.ac.uk</td><td colspan="2">Tel: 44 (0)28 9097 6476</td></tr>
<tr><td rowspan="3">Degree Pathway for which project is suitable (✓)</td><td>Medical Science</td><td>V</td><td colspan="2" rowspan="3"></td></tr>
<tr><td>Biochemistry</td><td>V</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>V

V</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">Cardiovascular disease and diabetes are the leading causes of death worldwide and is characterised by endothelial cell (EC) dysfunction. Replacing damaged ECs could be a potential therapeutic option but the availability of appropriate cell types has been a major limitation.
Recent ability to derive ECs from induced-pluripotent stem cells (iPS cells) holds huge therapeutic potential for personalised medicine and vascular cell therapy.
Recently, a new paradigm of direct reprogramming strategy has also been devised. We reasoned that, at earlier time points during reprogramming, we could direct the epigenetically activated cells which are induced by the iPS cell factors into lineage specific cell types such as ECs under defined conditions without traversing pluripotency[1].
However, the efficiency of cell reprogramming is very low and the underlying mechanisms remain unclear. In this study we have identified that the four reprogramming factors (OCT4, SOX2, KLF4, C-MYC) precisely activate Novel EC-Regulatory-Networks, which respond to specific stimuli such as Vascular Endothelial Growth Factor and Fibroblasts Growth Factor and enable EC reprogramming. This knowledge has allowed us to establish homogeneous populations of differentiated cells. Importantly, this work demonstrates the potential of reprogrammed ECs to enhance angiogenesis and neovascularisation. Together, these findings may establish the therapeutic potential of reprogrammed ECs which would have transforming consequences for regenerative and personalised medicine.

[1] Margariti (2012).PNAS 109,13793-13798.</td></tr>
</table>

Aims / objectives	This project will elucidate the signalling pathways which are regulated during the reprogramming of somatic cells to endothelial cell lineages using patients specific cells. **Experimental Design:** Patient specific Induced pluripotent stem cells and short reprogramming cells will be differentiated towards vascular cell lineages. The differentiation stage of the cells will be assessed in time point experiments by extracting RNA and Protein and further analysed, or stained and observed under a confocal microscope. Transfection experiments will be conducted to over-express potential genes which have an essential role in vascular cell differentiation. These studies will screen for and identify potential new therapies for vascular disease and regenerative medicine.
Techniques employed:	**The student will have the opportunity to gain expertise in cutting-edge research field of induced pluripotent stem cells technology:** 1. Pluripotent Stem cells and the powerful and novel approach of cell reprogramming; maintain them in undifferentiated conditions and induce differentiation towards endothelial cells. 2. Fundamental techniques in molecular biology such as RNA isolation and Real time PCR, protein extraction and western blot, confocal microscope to assess the differentiation stage of the vascular cells. 3. Transfection experiments and luciferase reporter assays to investigate the role of key signalling pathways implicated in vascular cell differentiation. Plasmid Purification. 4. Experimental design, data summary, critical thinking, analysis and interpretation of the results, presentation skills, scientific writing. Overall, the proposed project will be an opportunity for an enthusiastic student who would like to gain experience in the excited filed of stem cells and cell reprogramming and their potential use in regenerative medicine. It will be provided training in pluripotent stem cells laboratory skills, molecular biology, and cell signalling. They will collaborate in a multi-disciplinary research centre. These skills will be an important foundation for whatever career path the student decides to follow in the future.

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: **Medical Science**
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Development of survey to explore pharmacological and non-pharmacological airway clearance treatments in bronchiectasis.</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1.Prof Judy Bradley
Judy.bradley@qub.ac.uk
2. Dr Katherine O'Neill
k.oneill@qub.ac.uk</td></tr>
<tr><td>School / Centre</td><td colspan="4">Clinical Research Facility, Centre for Experimental Medicine, School of Medicine, Dentistry and Biomedical Science</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email:
Judy.bradley@qub.ac.uk</td><td colspan="2">Tel:</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">Bronchiectasis is a chronic respiratory condition with symptoms including difficulty clearing secretions as well as frequent chest infections and declining lung function. A core part of treatment is pharmacological (nebulized therapies and/or oral medications to enhance airway clearance) and non-pharmacological airway clearance treatments (for example a range of physiotherapy chest clearance techniques). Although these treatments are recommended in the guidelines, it is not clear how adherent patients are to these treatments or how frequently they are able to access their healthcare team. We have currently developed a patient questionnaire to explore pharmacological and non-pharmacological airway clearance treatments. This questionnaire is due to be launched on a patient driven European Lung Foundation website. In parallel with this, it is important to understand the prescribing patterns of healthcare team, with regards to pharmacological and non-pharmacological airway clearance treatments. Together, data obtained from these questionnaires will enable us to explore attitudes and habits of patients with bronchiectasis and the healthcare team caring for them. Additionally this data will direct the areas of further research in bronchiectasis.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">The aim of this project is to develop a questionnaire, to investigate physiotherapy use of Airway Clearance Treatments and their prescribing habits surrounding pharmacological and non-pharmacological Airway Clearance Treatments in Bronchiectasis. The developed questionnaire will eventually be used in a UK wide online platform to facilitate feedback.

The primary objective is to compile a provisional questionnaire regarding Airway Clearance Treatments in Bronchiectasis.
The secondary objective is to conduct a pilot test the questionnaire pack amongst experienced academic, research and clinical based physiotherapists to get their professional opinion regarding the content of</td></tr>
</table>

	the questionnaire and the language used in it, to ensure a user-friendly final version of the questionnaire. The methodology including recruitment will be facilitated by the academic supervisors. The feedback collected will direct changes to the questionnaire, allowing the final version of the questionnaire to be formed.
Techniques employed:	• The student will have the opportunity to work on a MRC funded study and exposure to studies conducted within the clinical trial research facility. • Questionnaire development • Interviews • Pilot testing • Online survey launch activity • Statistical analysis • Literature review

Honours Project for Intercalated BSc Degrees (2016-2017)

Intercalated BSc in: **Medical Science**
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Assessing using qualitative and quantitative criteria to assessment the quality of Lung Clearance Index data in bronchiectasis</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Dr Katherine O'Neill
k.oneill@qub.ac.uk
2. Prof Judy Bradley
Judy.bradley@qub.ac.uk</td></tr>
<tr><td>School / Centre</td><td colspan="4">Clinical Research Facility, Centre for Experimental Medicine, School of Medicine, Dentistry and Biomedical Science</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email: k.oneill@qub.ac.uk</td><td colspan="2">Tel:</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">Lung clearance index is an emerging outcome measure that is increasingly being used in respiratory clinical trials and also in some clinical sites to explore early lung disease.

As it is a new measure, it is essential that there is appropriate quality control measures in place to ensure validity of the assessment.

The supervisors on this project have received funding from MRC to explore various outcomes including the use of a novel lung function measurement (lung clearance index) in bronchiectasis. This study is running over 8 sites in the UK. Belfast is acting as the core facility for quality checking (over reading LCI measurements).

A significant amount of data has been collected in this study and is available for quality assessment.

A recent paper Jensen et al 2016 PLOS ONE 11(6), 1-9, have developed a checklist and stepwise approach to facilitate the review of each lung clearance index trial. These approaches include assessment of quantitative criteria as well as qualitative criteria.

This project has the potential to have an abstract output.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">The aim of this project will be to:
a. Become familiarised with the steps included in the qualitative and quantitative criteria as detailed by Jensen et al 2016.
b. Analyse the available data according to Jensen criteria.</td></tr>
</table>

	c. Compare the Jensen quality assessment to the current quality assessment procedure used.
Techniques employed:	1. The student will have the opportunity to work on a MRC funded study and exposure to studies conducted within the clinical trial research facility. 2. The student will become familiarised with lung clearance index which is a novel lung function measurement and increasingly being used as an important outcome in clinical trials. 3. The student will gain experience of how data is collected in multicentre clinical trials and transferred electronically to central sites. 4. The student will use a range of statistical techniques to summarise relevant data

Honours Project for Intercalated BSc Degrees (2016-2017)

Intercalated BSc in: **Medical Science**
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Exploring the relationship between Quality of life and lung function (FEV_1 and Lung Clearance Index) in Bronchiectasis (MRC funded clinimetrics project)</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">Prof Judy Bradley Judy.bradley@qub.ac.uk
Dr Katherine O'Neill k.oneill@qub.ac.uk</td></tr>
<tr><td>School / Centre</td><td colspan="4">Clinical Research Facility, Centre for Experimental Medicine, School of Medicine, Dentistry and Biomedical Science</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email:
Judy.bradley@qub.ac.uk</td><td colspan="2">Tel:</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">Bronchiectasis is a chronic respiratory condition with symptoms including difficulty clearing secretions as well as frequent chest infections and declining lung function. There are no licensed therapies for patients with bronchiectasis and it is not clear what outcome measures should be used in upcoming clinical trials. A large dataset of outcome measures including quality of life and lung function (FEV_1 and lung clearance index) has been collected from patients with bronchiectasis in the UK. Analysis of this database considering the relationship between quality of life and lung function (FEV_1 and lung clearance index), would yield an insight into the usefulness of these measures in monitoring patients with bronchiectasis.

Analysis of results would be suitable for abstract submission and presentation.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">The aim of this project will be to:
a. Review the quality of life questionnaires used in terms of their validity, reliability and responsiveness in bronchiectasis.
b. Become familiarised with lung clearance index data.
c. Analyse the relationship between lung function and quality of life</td></tr>
</table>

Techniques employed:	1. The student will have the opportunity to work on a MRC funded study and exposure to studies conducted within the Northern Ireland Clinical Research Facility. 2. The student will become familiarised with outcome measures in bronchiectasis used in clinical trials. 3. The student will gain experience of how data is collected as part of a clinical trial. 4. The student will use a range of statistical techniques to summarise relevant data.

Centre for Infection and Immunity

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Pharmacological inhibition of DREAM to normalise the inflammatory immune response in cystic fibrosis**			
Supervisor(s)	1. Dr Bettina Schock 2. Amal ElBanna			
School / Centre	Centre for Infection and Immunity			
Principal Supervisor's Contact Details	Email: b.schock@qub.ac.uk		Tel: 02890 972258	
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	x x	*Subject-specific awards* British Assoc Dermatologists Digestive Disorders Foundation Pathological Society Other ……	
Background information:	The ubiquitination protein A20 is an important negative regulator of the NF-kB pathway in inflammation. We have recently shown that A20 is reduced in Cystic Fibrosis (CF) chronic airway disease (epithelial cells). Further work indicated that the induction of A20 in CF might be repressed through increased expression of a repressor called DREAM and our recent ChIP data confirm a 'persistent binding of DREAM to its A20 promoter related binding site (DRE3 box). Through bioinformatical analyses of CF epithelial cells (connectivity mapping) we identified drugs predicted to reduce DREAM expression in CF epithelial cells and thereby to reduce CF airways inflammation.			
Aims / objectives	This project will further investigate the expression and the role of DREAM in CF epithelial cells after stimulation of the cells with bacterial products (e.g. LPS). It is hypothesized that pharmacological reduction of DREAM will normalise the pro-inflammatory phenotype of CF airway epithelial cells, basally and after stimulation with bacterial products. This will be tested in airway epithelial cells from patients with CF and non-CF controls after inhibiting/reducing DREAM expression using drugs predicted by connectivity mapping. A20 expression (mRNA and protein) as well as the inflammatory response of these cells will be analysed.			
Techniques employed:	Using epithelial cells (cell lines) with and without a CFTR mutation, we will use the following techniques: Tissue culture and sterile working techniques Quantitative real time PCR to detect A20, DREAM (and the A20 transcription factor USF1) mRNA Protein analyses for A20 and DREAM in treated cells using Western Blotting			

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Identification of the cytosolic DREAM binding protein in LPS stimulated cystic fibrosis epithelial cells.</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Dr Bettina Schock

2. Amal ElBanna</td></tr>
<tr><td>School / Centre</td><td colspan="4">Centre for Experimental Medicine</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email:
b.schock@qub.ac.uk</td><td colspan="2">Tel:
02890 972258</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>x</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>x

x</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 ubiquitination protein A20 is an important negative regulator of the NF-kB pathway. A20 is reduced in epithelial cells of patients with Cystic Fibrosis (CF) through increased expression of the repressor DREAM, which binds to the A20 promoter. Additionally, DREAM protein has cytosolic functions.
Nuclear DREAM normally occurs as a dimer or a tetramer and regulates gene expression but our preliminary data also suggest that cytosolic DREAM binds to an approximately 20 kD protein. Mass spectroscopy analyses indicated some binding partner candidates that could be involved in the transport of DREAM into the nucleus.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">This project will further investigate the composition of cytosolic DREAM in LPS stimulated epithelial cells. The student will use sterile tissue culture techniques to grow epithelial cells and will investigate the expression of our candidate DREAM binding partner using quantitative real time PCR and immunoprecipitation/Western Blotting.</td></tr>
<tr><td>Techniques employed:</td><td colspan="4">Using epithelial cells (cell lines) with and without a CFTR mutation, we will use the following techniques:
Tissue culture and sterile working techniques
Quantitative RT-PCR
Extraction of cytosolic proteins and protein analyses under non-reducing conditions for DREAM in using Western Blotting.
Transferable skills (presentations/communication skills, organisation of work, working alone and in a team).</td></tr>
</table>

Centre for Medical Education

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
~~Biochemistry~~
~~Microbiology~~

Project Title	How can we prepare medical students and foundation trainees for safe and effective practice? PROJECT 1			
Supervisor(s)	1. Tim Dornan 2. Richard Conn/Richard McCrory			
School / Centre	Centre for Medical Education, School of Medicine			
Principal Supervisor's Contact Details	Email: t.dornan@qub.ac.uk		Tel: 02890 975773	
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:	It is widely assumed that well designed undergraduate and foundation curricula can adequately prepare medical students and recently qualified doctors to practise safely, effectively, and happily. Evidence suggests otherwise. Efforts to strengthen curricula by intensifying teaching, assessment and introducing simulation have not yet proven successful. If you look at the nature of practice and the causes of clinical errors, that is unsurprising. Practice is far more complex than curricula suggest. Our group is investigating how people learn to prescribe (intravenous fluids, for example). We invite up to 2 intercalating students to join our team of medically qualified PhD students, social scientist, pharmacist, and senior education researcher. We will allocate two very motivated supervisors to each of them. Rather than specifying their exact projects now, we will tailor the projects to their individual wishes and needs. And according to where our research programme has reached, so that the research is very up-to-date. Interested students are invited to contact us for further information.			
Aims / objectives	• Methodically review relevant published articles relevant to a mutually agreed topic, probably related to prescribing but perhaps to some other topic in the domain of patient safety • Conduct a piece of primary research related to the same topic, examining how learning could be made more effective			
Techniques employed:	• Methodical literature survey; probably scoping review but, depending on the topic, an alternative methodology might be more appropriate • Depending on the topic and the interests of the student(s), this may include interviewing students, qualified professionals, or patients; it may involve observing real clinical or educational practice; or it may involve some form of experimentation • We hope the student(s) will present their work at conference(s); depending on the success of the project(s) these might also be published			

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
~~Biochemistry~~
~~Microbiology~~

Project Title	How can we prepare medical students and foundation trainees for safe and effective practice? PROJECT 2			
Supervisor(s)	1. Tim Dornan 2. Richard Conn/Richard McCrory			
School / Centre	Centre for Medical Education, School of Medicine			
Principal Supervisor's Contact Details	Email: t.dornan@qub.ac.uk		Tel: 02890 975773	
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:	It is widely assumed that well designed undergraduate and foundation curricula can adequately prepare medical students and recently qualified doctors to practise safely, effectively, and happily. Evidence suggests otherwise. Efforts to strengthen curricula by intensifying teaching, assessment and introducing simulation have not yet proven successful. If you look at the nature of practice and the causes of clinical errors, that is unsurprising. Practice is far more complex than curricula suggest. Our group is investigating how people learn to prescribe (intravenous fluids, for example). We invite up to 2 intercalating students to join our team of medically qualified PhD students, social scientist, pharmacist, and senior education researcher. We will allocate two very motivated supervisors to each of them. Rather than specifying their exact projects now, we will tailor the projects to their individual wishes and needs. And according to where our research programme has reached, so that the research is very up-to-date. Interested students are invited to contact us for further information.			
Aims / objectives	• Methodically review relevant published articles relevant to a mutually agreed topic, probably related to prescribing but perhaps to some other topic in the domain of patient safety • Conduct a piece of primary research related to the same topic, examining how learning could be made more effective			
Techniques employed:	• Methodical literature survey; probably scoping review but, depending on the topic, an alternative methodology might be more appropriate • Depending on the topic and the interests of the student(s), this may include interviewing students, qualified professionals, or patients; it may involve observing real clinical or educational practice; or it may involve some form of experimentation • We hope the student(s) will present their work at conference(s); depending on the success of the project(s) these might also be published			

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Healthcare professionals' experiences as immigrants to the UK and Ireland: a scoping review</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1.Mairead Corrigan

2. Jenny Johnston</td></tr>
<tr><td>School / Centre</td><td colspan="4">CME</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email:
m.corrigan@qub.ac.uk
j.l.johnston@qub.ac.uk</td><td colspan="2">Tel:</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</td><td></td></tr>
<tr><td>Background information:</td><td colspan="4">The student will use Arksey and O'Malley's scoping review framework to conduct a review of the empirical literature around immigration of health service students and personnel in the UK and Ireland. This is highly topical and will offer a first step towards supporting students as they tackle multiple cultural issues both in their professional and personal lives. This is an important part of a current stream of research looking at cultural diversity and medical training. The student's work will contribute to our knowledge on this important topic and help to develop appropriate support mechanisms.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">1. Map the current literature with regard to the research question
2. Identify gaps for potential future research</td></tr>
<tr><td>Techniques employed:</td><td colspan="4">Learn about different types of substantive literature review, including underpinning epistemology
Learn how to do database searching, manage large sets of results and synthesise results
Have the opportunity to submit a poster to a national conference in 17-18
Contribute to a peer-reviewed publication</td></tr>
</table>

Centre for Public Health

Honours Project for Intercalated BSc Degrees (2017-2018)

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">1. AJ McKnight

2. Postdoc starting in January 2017-2019</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>
</table>

	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 (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Gene-environment interactions in Age-related macular Degeneration</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">Amy Jayne McKnight & Ruth Hogg</td></tr>
<tr><td>School / Centre</td><td colspan="4">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: (0)28 9097 6359</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">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.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">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).</td></tr>
</table>

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

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Retinal evaluation in diabetic kidney disease – an early biomarker?**			
Supervisor(s)	1. Dr Gareth McKay 2. Prof Peter Maxwell			
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:	Clinical data and retinal images from the Northern Ireland Diabetic Retinopathy Screening Programme (NIDRSP) will be assessed with respect to renal function (serum creatinine; urinary albumin/creatinine ratio). These individuals will be stratified into two groups using estimated glomerular filtration (eGFR) equations. The stable kidney function group (chronic kidney disease CKD stage 1 and stage 2) are those individuals in whom eGFR measurements remained >60mL/min/1.73m^2 throughout the preceding 5 year screening period. Retinal vessel measurements in this "stable" kidney function group will be compared with retinal vessel data in individuals with progressive kidney failure. This "kidney failure" group will contain individuals in whom eGFR declined over 5 years to <60mL/min/1.73m^2. Retinal vessel measurements will then be correlated with risk of developing progressive diabetic kidney disease (DKD). This research will help determine if measuring the retinal microvasculature, as part of the diabetic retinopathy screening programme, would offer additional clinical utility in identifying patients at highest risk of developing renal failure. The retinal vasculature is directly accessible to direct and repeated non-invasive assessment enabling detection of early microvascular changes prior to clinically significant events. Recent improvements in digital retinal photography and *in silico* measurement have enabled improved characterisation of retinal vascular and structural parameters. **Improved non-invasive risk stratification for DKD** is a highly desirable prognostic clinical tool.			
Aims / objectives	We have a study ongoing that has recruited almost 300 participants. This study will collect and analyse retrospective data from NIDRSP to evaluate novel prognostic indicators for early identification of **individuals with diabetes at increased risk of renal decline**. Our analyses will determine if **retinal variation is associated with DKD in people with diabetes.**			

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 prospectively. 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. Logistic regression analysis will evaluate potential correlations between retinal microvascular variation and renal decline.

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

Project Title	**Can Autofluorescence be used as a non-invasive marker of outer retinal dysfunction in diabetic retinopathy**?			
Supervisor(s)	1. Ruth Hogg 2. Tunde Peto			
School / Centre	Centre for Public Health			
Principal Supervisor's Contact Details	Email: r.e.hogg@Qub.ac.uk		Tel: 028 90971654	
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:	Retinal auto fluorescence (AF) imaging has attracted much interest over the past 20 years as it provides a non-invasive method of assessing the accumulation of lipofuscin in the retinal pigment epithelium (RPE). Lipofuscin is a pigment that accumulates in the RPE during aging as a result of incomplete degradation of photoreceptor outer segments and is thought to mediate cell damage and senescence. Patterns of increased and decreased retinal AF have been observed in a variety of retinal diseases including diabetic retinopathy. However its clinical application has been hampered by the difficulty in making between-person comparisons due to the impact of ocular media changes not related to the retina on the absolute values. Recently a method has been incorporated within the commercially available Heidelberg Spectralis Scanning Laser Ophthalmoscopy that enables quantitative AF to be captured making cross-sectional comparisons more feasible. This project will investigate the relationship between qAF and both ageing and diabetic retinopathy to establish if qAF imaging could be used as clinical biomarker of outer retinal dysfunction in the development of Diabetic Retinopathy.			
Aims / objectives	1. Determine the relationship between qAF and age in a population based cohort 2. Investigate if the amount of qAF differs between those with diabetes but no DR compared to age-matched controls, and how does the amount of qAF differ between with increasing severity of DR 3. Clarify the relationship between the extent of qAF and other covariates which are related to more severe DR such duration of diabetes, body mass index, hbA1c			

Techniques employed:	Retinal grading, multivariate statistics, literature review.

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">What is the relevance of Peripheral retinal Autofluorescence in age-related macular degeneration and diabetic retinopathy?</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Ruth Hogg

2. Tunde Peto</td></tr>
<tr><td>School / Centre</td><td colspan="4">Centre for Public Health</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email:
r.e.hogg@Qub.ac.uk</td><td colspan="2">Tel: 02890971654</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">Autofluorescence imaging has been used clinically for a number of years to assess the accumulation of lipofuscin in RPE cells, a by-product of photoreceptor outer segment processing. It is thought that increased lipofuscin accumulation can occur as a result of both oxidative stress and inflammation, both important mechanisms in the development of age-related macular degeneration (AMD) and diabetic retinopathy (DR). The relevance of the peripheral retina in both conditions is being increasingly recognized but the role of peripheral autofluorescent patterns is not well understood. This project involves learning to evaluate Ultra-wide field retinal images for peripheral retinal Autofluorescent changes and investigating the relationship between these and traditional features of AMD and DR captured using conventional imaging. The data used will be from the Northern Ireland Cohort Longitudinal study of Aging (NICOLA) study.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">1. Characterize peripheral fluorescent changes in a population based cohort.
2. Investigate the relationship between peripheral autofluorescent changes and presence of AMD features.
3. Investigate the relationship between peripheral autofluorescent changes and presence of DR features.</td></tr>
</table>

Techniques employed:	Retinal grading, epidemiology, multivariate statistical analysis, literature review.

Honours Project for Intercalated BSc Degrees (2017-2018)

Intercalated BSc in: Medical Science
Biochemistry
Microbiology

<table>
<tr><td>Project Title</td><td colspan="4">Impact of maternal weight gain during and post-pregnancy on maternal insulin resistance and neonatal outcome</td></tr>
<tr><td>Supervisor(s)</td><td colspan="4">1. Dr Una Graham

2. Prof. David McCance</td></tr>
<tr><td>School / Centre</td><td colspan="4">Centre for Public Health</td></tr>
<tr><td>Principal Supervisor's Contact Details</td><td colspan="2">Email:
u.graham@qub.ac.uk</td><td colspan="2">Tel:
02890633423</td></tr>
<tr><td rowspan="3">Degree Pathway for which project is suitable (✓)</td><td>Medical Science</td><td>Y</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 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">Over 60% of pregnant mothers in Northern Ireland are overweight (BMI 25-30kg/m^2) or obese (≥30kg/m^2). Maternal obesity is a worldwide epidemic associated with a significant increase in maternal, fetal and neonatal complications including gestational diabetes mellitus (GDM). Offspring of mothers affected by GDM subsequently have an increased likelihood of diabetes and obesity at a young age. This transgenerational effect has the potential to create a vicious cycle with obesity and diabetes developing in future generations. Major public health efforts are needed to break this cycle. Whilst the association between maternal obesity and GDM is clear, the relative impacts of intra-pregnancy, inter-pregnancy and immediate post-natal weight changes on insulin sensitivity during and post-pregnancy have not been reported. This data would enable public health strategies to be directed towards women at a time when they, and their future offspring, are most likely to benefit from intervention.</td></tr>
<tr><td>Aims / objectives</td><td colspan="4">1. To determine the impact of maternal weight changes at 3 time points on insulin sensitivity (as measured by the insulin response during the oral glucose tolerance test). Timepoints: 1. From early pregnancy (<14weeks gestation) to late second trimester (24-28 weeks gestation), 2. From early pregnancy (<14 weeks) to early post-pregnancy (within 8 weeks of delivery) and 3. From index pregnancy (<14 weeks) to subsequent pregnancy (<14 weeks)

2. To assess the impact of maternal weight changes and insulin sensitivity on neonatal weight and outcome</td></tr>
</table>

Techniques employed:	This study will enable the student to develop extensive skills in data extraction, processing and interpretation; key skills for clinical research. The student will be given an honorary contract within the BHSCT and have the opportunity to attend specialist diabetes in pregnancy clinics, and education sessions within the Regional Centre for Diabetes and Endocrinology. Data relating to maternal weight changes, biochemical results and neonatal outcome will be extracted from clinical databases and combined with data from paper records to generate an extensive dataset of women evaluated for GDM over the past decade. To assist with this the student will be given the opportunity to attend training in both excel and SPSS. Data analysis will be performed by the student supported closely by the project supervisors and biostatisticians in the CPH. It is anticipated that the student will present their results at local and National conferences in Diabetes (Irish Endocrine Society Annual Meeting, Diabetes UK Annual Conference); and assist in the preparation of a manuscript for International publication.