DCAT Vacation Studentships 2021

| Project Number | Title and Description | Supervisor |
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| 1 | **Title: Combining genetic, molecular and imaging data to understand the causes of mental illness**<br><br>Genetic studies have identified hundreds of regions of DNA which can affect an individual's risk of developing mental disorders such as schizophrenia and bipolar disorder, but for the majority of these the mechanisms by which they act are unknown. Imaging studies have identified structural and functional differences between patients with mental illness and controls, but it is frequently not clear whether these differences are responsible for disease development, or consequences of the disease. The aim of this project will be to use genetic information, combined with molecular data from post-mortem brain samples, to identify brain regions and processes involved in the development of mental illness. We will use computational methods to identify the relevant genes, together with the implicated brain region, and combine these results with the brain imaging literature to develop a deeper understanding of the causes of mental illness. | **Dr Andrew Brown**<br>**Principal Investigator**<br>**Division of Population Health and Genomics** |
| 2 | **Title: Analysis of patient reported outcome measures through a novel diabetes self-management platform**<br><br>Diabetes prevalence is rapidly increasing globally and effective interventions are required to mitigate the associated spiralling individual and health service costs. My Diabetes My Way (MDMW) was launched in 2008 and is Scotland's interactive website and mobile app for people with diabetes and their carers. The service contains multimedia resources for diabetes education, structured eLearning courses and offers access to electronic personal health records. This allows us to link routinely collected clinical results with data entered by users, including structured patient reported outcome measures (PROMs – e.g. PHQ-9, WHO-5). The aim of MDMW is to support diabetes self-management, enhance communications between people with diabetes, their carers and healthcare teams and to support shared decision-making.<br><br>For this project, we aim to analyse PROMs data that has been collected since mid-2019, alongside routinely collected clinical outcomes to understand how changes in in wellbeing and mental health scores are associated with changes in key diabetes care processes, such as HbA1c, weight and blood pressure. | **Dr Scott Cunningham**<br>**Senior Lecturer**<br>**Division of Population Health and Genomics** |

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| **3** | **Title: Analysis of activity data through a novel diabetes self-management platform**<br><br>Diabetes prevalence is rapidly increasing globally and effective interventions are required to mitigate the associated spiralling individual and health service costs. My Diabetes My Way (MDMW) was launched in 2008 and is Scotland's interactive website and mobile app for people with diabetes and their carers. The service contains multimedia resources for diabetes education, structured eLearning courses and offers access to electronic personal health records. This allows us to link routinely collected clinical results with data from personal devices such as activity trackers. The aim of MDMW is to support diabetes self-management, enhance communications between people with diabetes, their carers and healthcare teams and to support shared decision-making.<br><br>For this project, we aim to analyse activity data that has been collected since mid-2019, alongside routinely collected clinical outcomes to understand how activity affects key diabetes care processes, such as HbA1c, weight and blood pressure. | **Dr Scott Cunningham**<br>**Senior Lecturer**<br>**Division of Population Health and Genomics** |
| **4** | **Title: Clinician experiences and expectations of a novel diabetes self-management platform**<br><br>Diabetes prevalence is rapidly increasing globally and effective interventions are required to mitigate the associated spiralling individual and health service costs. My Diabetes My Way (MDMW) was launched in 2008 and is Scotland's interactive website and mobile app for people with diabetes and their carers. The service contains multimedia resources for diabetes education, structured eLearning courses and offers access to electronic personal health records. The aim of MDMW is to support diabetes self-management, enhance communications between people with diabetes, their carers and healthcare teams and to support shared decision-making.<br><br>For this project, we aim to analyse the responses to a survey where data were collected detailing healthcare professionals' experiences with patients who have used the MDMW service. It also explores their expectations for a service that supports patient self-management. The mixed methods analysis will deal with both qualitative and quantitative data and involve thematic analysis using tools such as nVivo. | **Dr Scott Cunningham**<br>**Senior Lecturer**<br>**Division of Population Health and Genomics** |
| **5** | **Title: Is metabolic-associated (non-alcoholic) fatty liver disease (MALFD/NAFLD) underdiagnosed in patients with diabetes mellitus?**<br><br>Non-alcoholic fatty liver disease (NAFLD), recently renamed metabolic-associated fatty liver disease (MAFLD), is a common cause of chronic liver disease in developed countries. There is a significant link between type 2 diabetes mellitus and MAFLD, yet MAFLD is often underdiagnosed in this patient group. This project will involve reviewing clinical records to investigate the rates of diagnosed and undiagnosed MAFLD in primary and secondary care diabetes follow-up clinics. We will use this data to inform future development of a MAFLD screening tool for high-risk populations. There will also be the opportunity to explore how a large NHS Blood Sciences laboratory operates, and to learn about diabetes, liver disease and biochemistry. | **Professor John Dillon**<br>**Professor of Hepatology and Gastroenterology**<br>**Division of Molecular and Clinical Medicine** |

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| **6** | **Title: How has the Enhanced Liver Fibrosis score impacted the intelligent Liver Function pathway?**<br><br>The intelligent Liver Function Testing pathway is an award-winning, algorithm-driven investigation pathway for liver disease. It combines clinical details and blood test results to generate a diagnosis and management plan which can be returned to the requesting GP. The degree of liver fibrosis (scarring) was previously estimated using calculated fibrosis scores, but a new blood test, the Enhanced Liver Fibrosis (ELF) score, has since been introduced. This project will investigate what effect the ELF score has had on referrals to the liver clinic and patient outcomes by reviewing laboratory results and clinical records. There will also be the opportunity to explore how a large NHS Blood Sciences laboratory operates, and to learn about liver disease and biochemistry. | **Professor John Dillon**<br>**Professor of Hepatology and Gastroenterology**<br>**Division of Molecular and Clinical Medicine** |
| **7** | **Title: Exploring the relationship between T2D and Parkinson's Disease**<br><br>Among the many clinical complications associated with type 2 diabetes it being increasingly recognised that the health of the brain is also affected. A growing number of studies have demonstrated links between T2D and Parkinson's disease, a chronic degenerative brain disease affecting coordination of muscle movement. Serum biomarkers for Parkinson's disease are also being developed with one of the most promising among these being alpha-synuclein.<br><br>For this project you will join my research group and by making use of pre-existing clinical datasets linked to genetic data within a SafeHaven environment you will be able to explore the relationship between T2D and Parkinson's Disease. You will have access to statistical software by making use of pre-written building blocks of code for analysis. Previously measured serum alpha synuclein levels are available in a relatively small number of individuals and it will be possible to investigate how clinical parameters affect serum alpha-synuclein levels and its association with Parkinson's disease. This project will provide a number of important skills in healthcare data science. A successful project by a committed student could lead to a presentation of the findings at a national scientific conference and a potential publication. | **Dr Alex Doney**<br>**Clinical Senior Lecturer**<br>**Division of Population Health and Genomics** |
| **8** | **Title: Improving clinical trial efficiency in Tayside**<br><br>Clinical trials, particularly randomised controlled trials, are central to the identification and practice of evidence-based medicine. They are, though, complex and costly to undertake. Clinical Trials Units (CTUs) are specialist units which have been set up to design, conduct, analyse and publish clinical trials and other well-designed studies, in collaboration with clinical scientists (https://www.ukcrc-ctu.org.uk/page/CTURole). They provide an essential service to medical research, but face challenges around funding, bureaucracy and the practical issues of clinical medical research (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5759880/). We need continual research, audit and review of research methodology to hone the efficiency of CTUs, and their ability to conduct and deliver results that will impact on clinical practice.<br><br>Tayside Clinical Trials Unit (TCTU) is a UK Clinical Research Collaboration (UKCRC) registered CTU, established in 2008, managing a range of clinical studies, from inception to completion. We now seek to conduct research into how the management of trials matches the needs and expectations of clinical researchers and other stakeholders. This project will aim to collect information from clinical researchers involved with TCTU on what they want and expect from TCTU, and how this matches reality. | **Dr Sarah Inglis**<br>**Senior Clinical Trial Manager**<br><br>**Professor Blair H. Smith**<br>**Clinical Co-director**<br><br>**Tayside Clinical Trials Unit** |

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| | This will be compared with information collected on the mechanisms governing TCTU, seeking areas of positive and negative alignment, particularly those where change is both possible and potentially beneficial. This work will inform the development of a tool to guide ongoing service improvement, and greater efficiency in clinical research around Tayside. This development could form part of an extension of this project.<br><br>The student will survey/interview researchers from a range of clinical backgrounds, and trial/data managers and coordinators in TCTU. S/he will critically review the processes and procedures necessary to conduct clinical research, identifying areas of potential change. These activities will provide the opportunity to gain an in-depth understanding of how clinical research is conducted in the real world, and introductions to many of the people active in this field locally. | |
| **9** | **Title: Interaction between HFpEF and AF: Further insights through use of genetic risk scores**<br><br>Atrial fibrillation (AF) and heart failure with a preserved ejection fraction (HFpEF) are closely intertwined disorders that afflict millions of people, many of whom are obese or have diabetes mellitus or other proinflammatory conditions. Conceivably, the convergence of AF and HFpEF might be explained by 2 distinctly different frameworks. On the one hand, it is possible that each phenotype might lead sequentially to the other (ie, the increased left ventricular [LV] filling pressure in HFpEF may cause left atrial [LA] dilatation that triggers AF, and conversely, the rapid heart rate that accompanies AF might lead to LV fibrosis, although there is little evidence to support this hypothesis). On the other hand, the 2 disorders may be parallel manifestations of the same underlying myocardial disease, which causes AF (because it affects the LA) and HFpEF (because it afflicts the LV). Recent genome-wide association studies (GWAS) have demonstrated that AF and HF are complex disorders with polygenic architectures. Despite overlap in potential top risk loci, the genetic susceptibility to both AF and HF is likely to involve the aggregate contributions of hundreds or thousands of loci, consistent with other polygenic conditions. To understand whether genetic risk of AF is an important and potentially useful determinant of HFpEF, we will analyse HFpEF from the GoDARTS and other available with genome-wide genotyping data and compare genetic risk factors for AF and HF to ascertain the extent to which heritable risk of HF is explained by genetic risk factors for AF. | **Professor Chim Lang**<br>**Professor Cardiology**<br>**Head of the Division of Molecular and Clinical Medicine**<br><br>**Dr Ify Mordi**<br>**Clinical Senior Lecturer**<br>**Division of Molecular and Clinical Medicine** |
| **10** | **Title: Use of Genomics to Untangle Conundrums in Heart Failure**<br><br>Why do some patients respond well to heart failure treatment with ACE inhibitors and beta-blockers, whereas others get no benefit, despite similar clinical features? Is it possible that genetics might underlie some of these differences?<br><br>This project is a database study which will focus on outcomes in patients with heart failure. The student will develop genetic risk scores for relevant comorbid conditions such as coronary artery disease, hypertension and heart failure and will determine whether genetic risk of these conditions is associated with the likelihood of response to heart failure therapy.<br><br>The student will gain skills in data cleaning and analysis, statistics and will produce a paper which they will be first author on during the project. As a data project supervision and analysis can be conducted remotely. | **Dr Ify Mordi**<br>**Clinical Senior Lecturer**<br>**Division of Molecular and Clinical Medicine** |

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| **11** | **Title: Study of the oral microbiome in Inflammatory Bowel Disease patients**<br><br>Chronic Obstructive Pulmonary Disease (COPD) and Inflammatory Bowel Disease (IBD) share many features. They are both chronic inflammatory conditions of mucosal surfaces with no cure, and for which medical therapy can be sub-optimal.<br><br>It has been recognised for some years that patients with IBD may present with pulmonary disease, and also that some patients may develop pulmonary disease which pre-dates the onset of their IBD. For both conditions, it is now accepted that there are three common drivers; a genetic predisposition, an environmental trigger, and dysregulation of the resident microbiome.<br><br>COPD and IBD display similarities in the observed dysregulation of the microbiome, with a reduction in bacterial diversity observed with active inflammation and common strain-specific shifts. These observations suggest the possibility of a common environmental trigger. The respiratory tract and the intestinal tract share a common portal of entry for environmental triggers – the mouth. Mouth ulcers are a common feature in patients with active intestinal Crohns disease – but the aetiology of these is poorly understood.<br><br>Emerging data suggests that bacteria of oral origin are associated with inflammation in extra-oral sites<br>We wish to study the oral microbiome of patients with a diagnosis of IBD and compare with historical reference samples from healthy controls and COPD patients. Sampling saliva is a well validated means of surveying the oral microbiome via 16S rRNA sequencing.<br><br>Methods<br>Patients attending the IBD clinic with active disease or admitted to hospital with active IBD will be studied (N=50 for an initial pilot study). Patient demographics and IBD phenotype will be recorded, and any associated respiratory diagnosis. A questionnaire will survey patients for respiratory symptoms. Individuals who have received antibiotics in the previous 2 weeks will be excluded. In parallel a matched cohort of healthy controls without respiratory disease or GI disease will be enrolled.<br>Oral wash samples will be obtained from patients with active IBD (Crohns disease and ulcerative colitis).<br><br>Students will gain experience of clinical research and the importance of accurate data collection, careful sample collection and processing, and insight into microbiome research at the cutting edge. | **Dr Craig Mowat**<br>**Clinical Senior Lecturer in Gastroenterology**<br>**Division of Population Health and Genomics**<br><br>**Prof James Chalmers**<br>**Chair of Respiratory Research**<br>**Division of Molecular and Clinical Medicine** |
| **12** | **Title: Pharmacogenetics of digoxin toxicity**<br><br>Digoxin is an old drug that remains widely used to achieve rate control in atrial fibrillation and has potential therapeutic benefit in heart failure due to its positive inotropic action. It has a narrow therapeutic index and has many potential drug-interactions. Its use is associated with increased mortality in some patients, with drug levels after initiation predictive of adverse outcome. Digoxin is primarily transported by the transporter P-Glycoprotein (P-GP, otherwise called Multidrug resistance protein 1 (MDR1) encoded by the *ABCB1* gene). The studies done to date have been limited to small pharmacokinetic studies and pharmacoepidemiological studies. The recent release of UK Biobank primary care data on ~260K individuals allows the investigation of how genetic variants that alter digoxin transport impact on risks of harm from digoxin. | **Professor Ewan Pearson**<br>**Professor of Diabetic Medicine**<br>**Head of the Division of Population Health and Genomics** |

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| | This pharmacogenetic project will identify individuals treated with digoxin and a matched comparator group and assess how genetic variants in ABCB1 alter risk of cardiovascular and all-cause mortality, as well as the risk of Digoxin toxicity (captured in the primary care codes or hospital discharge codes). If time allows, we will investigate other clinical parameters (such as renal function and electrolytes) and how these interact with genetic variants on the risk of digoxin harm.<br><br>The study will all be undertaken in the Health Informatics Safe Haven and the student will work closely with statisticians in the Pearson group. The student should have an interest in data analysis and will need to learn the basics of 'R' programming. The student will learn how to undertake survival modelling and logistic regression models and how to incorporate genetics into these models. | |