THE UNIVERSITY of York

C2D2 Centre for Chronic Diseases & Disorders

C2D2 Projects funded from First Round

Dr Dawn Coverley, Biology
Analysis of variant Ciz1 in pre and post-treatment plasma samples from lung cancer patients attending York hospital

Lung cancer is responsible for more than 1 million deaths each year, more than breast, colon and prostate cancer combined. C2D2 funding will be used to evaluate a potential post-treatment niche for employing a biomarker that can report on reduced tumour burden or on recurrence as part of a wider international research project on screening for the cancer.

Dr Chris Elliott (PI), Biology; Prof Alex Wade, Psychology
Dynamic measurements of neural gain control and visual processing in drosophila models of neurological disease.

Human vision can be affected by diseases of the central nervous system—for example, epilepsy, Parkinson's disease and dementia. In some cases, these diseases can be traced to mutations in a single gene and, remarkably, mutations of the counterparts of these genes in fruit flies cause conditions that resemble the human disease. This project seeks to understand the effect that single gene mutations have on neural function in both humans and flies. The data acquired will help in diagnosing, understanding, modelling and treating human neurological disease.

Prof Deborah Smith (PI), Biology; Prof Paul Kaye, HYMS, CII
Establishment of sandfly colonies to support research on leishmaniasis

The leishmaniases are neglected tropical diseases that threaten public health in 88 countries around the globe. York is at the forefront of both fundamental and translational research on the leishmaniases, with well-advanced projects focusing on new drugs and vaccines for these chronic diseases. This funding will be used to establish and maintain colonies of the sandfly vector in York for studying parasite development and transmission to man, both essential processes in the spread of disease which, if blocked, would prevent leishmaniasis.

Dr Gavin Thomas (PI), Biology; Prof Jennifer Potts, Biology
Elucidation of the structure of a YD-repeat containing virulence protein from the chronic pathogen Pseudomonas aeruginosa.

This project aims to contribute to our understanding of why certain bacteria, particular ones that cause chronic infections in patients with the genetic disease cystic fibrosis, can persist for so long. It follows on some research conducted on a family of proteins that appear to be involved in allowing bacteria to stick to other cells or even kill other cells using a toxin presented at the tip of the protein – a toxin on a stick. Computational and experimental methods will be used to try and determine what the repeating elements that are believed to make up this 'stick' look like and to learn more about what their function is.

Dr Fabiola Martin, HYMS, CII; Dr Robert Newton, Health Sciences
From York to Malawi and back: The first UK based sero-prevalence study of Human T lymphotropic virus 1/2 in paired mothers and children living in Malawi.

Human T lymphotropic virus type 1 (HTLV-1) chronically infects human immune cells and can lead to debilitating disease or blood disorders. HTLV-1 is commonly found in the West Indies and Southern Japan. Sub-Saharan Africa is thought to be a high endemic area, but it is not mapped sufficiently to allow the promotion of effective HTLV prevention programs, such as ante-natal and blood transfusion screening. In a collaboration between Centre of Immunology and Infection and the Epidemiology and Genetics Unit (Health Sciences), this project aims to test 1000 paired Malawian mother-child blood samples to gather data on incidence, transmission rate and co-infections and malignancies.

Dr Dimitris Lagos (PI), Biology, CII; Prof Jonathan Timmis, Computer Science
Dissecting RNA interactions in disease: from modelling gene networks to future therapies

Significant changes in the abundance of individual proteins within a cell can result in faulty cellular functions. An accumulation of such functions leads to disease. This project will combine cutting edge molecular biology studies with computational modelling to understand the processes that cause these changes in a group of key proteins known as RNA-binding proteins or RBPs. This study will form the basis for further comprehensive investigations in the role and characterisation of RNA networks in disease.

Dr Marjan van der Woude (PI), Biology, CII; Dr Roderick Vann, Physics; Prof Jennifer Potts, Biology; Dr Anne-Kathrin Duhme-Klair, Chemistry; Dr Anne Routledge, Chemistry
Assessment of the activity of novel antimicrobial therapies against bacterial biofilms: establishing a resource to support non-microbiologists

Biofilm growth of bacteria, a mode of growth particularly associated with chronic infections, can confer drug resistant behaviour, complicating treatment of infections. The project brings together microbiology expertise (Van der Woude, CII) to test effectiveness of novel antimicrobial therapies under development, specifically: modifying drugs to circumvent resistance (Duhme-Klair and Routledge, Chemistry), identifying bacterial targets for biofilm inhibiting agents (Potts, Biology), and biomedical plasmas (Plasma Institute). An additional aim is to support the establishment of a University "biofilm interest" network through which resources and strategies can be shared, and encourage the development of complementary strategies.

Dr Tim Andrews (PI), Psychology; Prof Andy Young, Psychology
Mapping the functional organization of the temporal lobes with fMRI

Despite the fact that highly disabling disorders, such as autism and schizophrenia, are typically associated with abnormalities in the temporal lobes, the functional organization of this region is not well understood. This project aims to develop novel analysis methods to improve our understanding, using the expertise available at York. This analysis will be based on an existing database of the brains of over 150 normal participants and will provide a normative range to compare with individuals with autism or schizophrenia.

Prof Antony Morland (PI), Psychology; Prof Alex Wade, Psychology; Dr Heidi Baseler, HYMS
Understanding human visual cortical connectivity in health and chronic disease

This project will draw on local expertise in analysing Functional Magnetic Resonance Imaging (fMRI), and apply it specifically to the human visual system. Specifically the project will investigate how the spatial pattern of brain connections in the visual cortex changes during development as well as in subjects rendered blind by disease of the eye. The aim is to answer these important scientific questions at the same time as creating a new, freely-available scientific tool that will empower the larger community of neuroimagers at York to perform cutting edge research in the future.

Dr Deborah O'Connell (PI), Physics; Prof Norman Maitland, Biology; Prof Timo Gans, Physics; Dr Erik Wagenaars, Physics
Plasmas: A key enabler for cancer therapeutics?

The unique properties of cold non-equilibrium plasmas have been identified as having enormous potential in, for example, disease therapeutics and plasma pharmacology as drug alternatives. This project will seek to identify how this technique can be exploited to eradicate the cancer stem cells that are believed to be the tumour initiating cells and also the seed to radio-resistance in prostate cancer. The pooling of world-class expertise and facilities across departmental boundaries will generate internationally unique capabilities, placing the University of York at the frontier of this emerging field.

Dr Fiona Polack (PI), Computer Science; Prof Norman Maitland, Biology; Prof Susan Stepney, Computer Science
Data and simulation of the dynamics of stem cell amplification in prostate disease development and control (Benign Prostatic Hyperplasia)

Computer simulation can be used to complement purely biological approaches to explore dynamically the complex nature of cell division and differentiation. Benign prostatic hyperplasia (BPH), a non-malignant expansion of the prostate with no known cause, is the major chronic disease of the ageing male population. Previous cancer studies undertaken at York have shown that BPH may result from persistent expansion of stem cells. The project will adapt a state-of-the-art simulator to explore the stromal cell dynamics implicated in BPH and to simulate the effects on cell dynamics of new BPH drug treatments, in advance of or in parallel with clinical trials.

Dr Patrick Johnston (PI), Psychology; Dr Barry Wright, HYMS
Are time-perception abnormalities linked to social and motor impairment in Autism Spectrum Disorder?

Autism Spectrum Disorder (ASD) is a complex developmental disability that leads to problems with communication and social interaction. Recently, researchers have found that individuals with ASD often have a poor sense of time. The goal of this project is to see how the ability to perceive time is linked to other problems in ASD. A study will be set up to test for differences between individuals with ASD and a matched control group on a variety of measures including tests of time perception, social perception and the ability to imitate (mimic) the actions of others. This will be the first step in setting up a new multidisciplinary research group to test ideas relating to ASD.

Dr Henrice Altink (PI), History
Tuberculosis in the colonial and independent British Caribbean

The aim of this project is to assess the possibility of an externally-funded international research network on the role of race and ethnicity in the prevention, control and treatment of Tuberculosis (TB) in the British Caribbean in the decades preceding and following independence, which will operate alongside the investigator's study of TB in Jamaica. A workshop will be hosted to determine interest in and advocate the possibilities of such a research network to potential UK collaborators. Time will also be spent in Jamaica, Barbados and Trinidad to scope archival sources on TB, meet with potential collaborators at the University of the West Indies and explore the possibility of conducting oral history.

Dr Richard Cookson (PI), Centre for Health Economics; Dr Steven Oliver, HYMS
Incorporating health inequality concerns into performance monitoring and economic evaluation – feasibility study in colorectal cancer and collaboration building meetings

Funding will be used to prepare three large inter-disciplinary grant bids to incorporate health inequality concerns into the performance monitoring and economic evaluation tools that NHS policy makers and managers use to guide their decision making. The main task will be to demonstrate that it is feasible to monitor the contribution of the NHS to tackling health inequality in one specific "pilot" area of colorectal cancer. The project will assemble a multi-disciplinary team of economists, epidemiologists and public health specialists, drawing together expertise from the Centre for Health Economics, the Department of Health Sciences, the Yorkshire and Humber Public Health Observatory, the Northern and Yorkshire Cancer Registry and Information Service, and Leeds Institute for Molecular Medicine.

Dr Elizabeth Hughes (PI), Health Sciences; Dr Fabiola Martin, CII
Scoping Project for Opt Out Blood Bourne Virus and Sexually Transmitted Infection testing in psychiatric inpatient units

Many people are unaware of having been infected with a sexually transmitted infection (STIs) and/or blood borne virus such as HIV and Hepatitis B and C. Early identification means that treatment can commence immediately which in turn helps prevents disease progression, further transmission and dramatically improves life expectancy. Evidence from the USA and mainland Europe indicates that people with long term mental health problems are more at risk of STIs than the general population, however mental health services do not routinely offer sexual health promotion or testing. Surprisingly this is an under-researched area in the UK and there is an urgent need for in-depth developmental work to support a larger,

external proposal. The overall aim of a future research programme would be to develop and evaluate a STI testing service within mental health inpatient units. This initial scoping work will develop collaborations with experts and service user groups as well as a background literature review in order to prepare a proposal for primary research.

Prof Jane Thomas-Oates (PI), Chemistry; Dr Jenny Southgate, Biology
Identification of metabolites mediating wound healing in bladder epithelium

Chronic disorders of the bladder are common and age-related, encompassing both cancer (7th commonest and most expensive to treat) and benign dysfunctional disorders (stress urinary incontinence, overactive bladder and painful bladder syndromes). This project aims to identify, using state-of-the-art chemical analysis approaches, the signalling molecules that are believed to be released from the cells of the bladder lining when damaged and which, it is predicted, are important in regulating both normal bladder function and repair. This new understanding is important for developing new therapies to resolve dysfunctional disorders and repair diseased or damaged bladders.