

Summaries of Procedures Project Licences approved by AWERB across 2023

PPL.1Feb23

Aims: To gain greater understanding of blood vessel glycocalyx biology in health and disease so that targeted therapeutics can be developed.

Benefits: Dysfunction of the glycocalyx is a contributing factor in several important diseases including diabetes, kidney disease, atherosclerosis, and sepsis. The purpose of the outlined work is to advance understanding of the molecular mechanisms underlying the formation and maintenance of the glycocalyx. This may help guide the development of therapeutic interventions that could be used to restore its integrity and thereby reduce the severity and improve the outcome of diseases for which glycocalyx dysfunction plays a contributing role

Harms: Rats and mice (mainly) used. Described as largely mild procedures and some moderate. This is stated because lots of interventions are non-invasive or terminal and disease models are refined. Harms include inducing disease state (diabetes, sepsis), surgery

PPL.1Mar23

Aims: To define mechanisms through which genes linked with the risk of psychiatric disease impact brain activity and behaviour. The findings will be integrated with clinical work in humans to inform new diagnosis and treatment approaches for schizophrenia and related disorders.

Benefits: Back-translation of signatures of abnormal brain activity and cognition from people at links with clinicians, patients and industry.

Harms: GA mice/rats (carrying mutants that simulate copy number variants), behaviour tests and surgical procedures, to either attach electrodes to the skull for EEG recordings or to implant electrodes into selected brain regions for multiple single neuron population recordings. Prospective severity mild and moderate.

PPL.1Jun23

Aim: To evaluate ways of enhancing the protection of the heart of children during cardiac bypass surgery.

About 1% of babies are born with a defective heart and some of these may have to undergo heart surgery to correct the defect, often whilst they are still very young. During surgery, it is often necessary to stop the heart temporarily to enable the surgeon to repair the defect. During this period, the blood supply to the baby's vital organs is maintained by coronary bypass. Despite this while the heart is stopped, and in the period immediately after it is restarted, the heart can sustain damage that can permanently restrict its function. The techniques currently used to limit this damage are based on those developed for adult patients however, these are less effective in children. Therefore, there is a need to develop more effective ways of protecting the heart of children's during heart surgery.

Benefits: The primary output of the study will be new data relating to the mechanisms by which infant heart tissues sustain damage during coronary bypass surgery. In addition, the study will produce data relevant to the assessment of interventions aimed at minimising heart tissue injury during surgery.

Harms: Pigs, coronary bypass under terminal anaesthesia (non-recovery), minor heart defect induced under anaesthesia with recovery (moderate), split approximately 50/50.

PPL.2Jun23

Aim: The aim of this project is to assess the potential of delivering drugs to the central nervous system (CNS) using natural fluid drainage pathways and to facilitate the development of the technology needed to achieve this.

Benefits: Diseases of the central nervous system are a major cause of suffering and death. There is a lack of effective treatments for many diseases of the CNS.

A major obstacle to the treatment of diseases of the CNS is the difficulty in achieving therapeutic drug concentrations required locally. Most drugs used in the treatment of diseases are prevented from entering the CNS by the blood brain barrier. As a result, the development of effective treatments for brain tumours and neurodegenerative diseases such as dementia, Parkinson's, Alzheimer's and Motor Neurone Disease had been severely limited. Therefore, there is an urgent need to develop drug delivery systems that can overcome the limitations imposed by the blood brain barrier in order to address the unmet clinical need of patients.

Harms: Pigs, sheep, surgery. Imaging, largely moderate procedures.

PPL.1Jul23

Aims: To advance understanding of how neural processing within the cerebellum and its interconnections with the rest of the nervous system controls behaviour, including higher brain functions of cognition and emotion.

Harms: Rats and mice, all moderate, surgery, injection of neuroactive substances into brain, probes, miniscopes, and other interventions non aversive and aversive behaviour tests, food/water restriction.

Benefits: The outlined studies will generate data relevant to advancing understanding of the neural processes that underpin behaviour. In the longer term, it is to be hoped that by advancing knowledge in this field, the work will contribute to the identification of improved treatments for patients suffering from a range of conditions involving cerebellar defects, such as spinocerebellar ataxias and essential tremor and generalised anxiety disorder.

PPL.1Sept23

Aims: To develop more effective interventions (including novel therapeutic agents, stem cell and tissue engineered conduits) for the treatment of heart disease (reducing severity of restenosis) and to generate the data required to obtain approval for progression into first in human clinical trials.

Benefits: The primary output of this project will be data on the performance, safety and efficacy of novel interventions/products for the treatment of vascular diseases (e.g. novel designs of stents, grafts & valves).

Harms: The studies will be undertaken using juvenile and adult pigs and sheep as their cardiovascular system closely resembles that of humans in both structure and size. Animals

will experience at least one surgery (and up to two) under general anaesthetics plus imaging. Moderate severity.

PPL.1Oct23

Aims: The aim of this project is to have a better understanding of immune responses to an infectious disease which causes cancer and suppression of immune response in chickens.

Benefits: Determine the immunogenicity and efficacy of cell-free vaccine and other novel vaccine candidates against Marek's disease.

Harms: Chickens, moderate procedures

PPL.1Nov23

Aims: To determine the efficacy of therapeutic interventions for atherosclerosis and atherosclerotic aneurysms using representative mouse models (prior to progression into large animal models). Mice will be used in all studies to determine the effectiveness of immune modulating approaches upon atherosclerosis and its complications.

Benefits: The data generated from the studies within this project will demonstrate if targeting immune cells and their products protect against atherosclerosis. If successful, this project will highlight potential therapeutic targets alongside possible biomarkers of disease progression, and therefore support their advancement into trials or safety and effectiveness assessment in large animal models.

Harms: Mice, adverse effects described as largely moderate, they may be fed high fat diet, be administered agents such as angiotensin 2 to hasten aneurysm and treatments, may have surgery or implanted devices

PPL.2Nov23

Aims: Develop new or improved bone marrow stem cell-based therapies for patients with neurological disease, and to determine the precise ways in which bone marrow-derived cells protect and/or repair nerve cells in multiple sclerosis, genetic ataxias, and Alzheimer's disease

Benefits: This project will help advance knowledge of the molecular and cellular processes that occur in response to nerve cell injury. It will also give insights into the protective and regenerative mechanisms of adult stem cell populations and how these processes may be manipulated to improve nerve cell repair and achieve functional recovery.

Harms: Largely mice, with a small proportion of rats. 50% mild, 30% moderate. 20% severe
Dosing, Surgery (cranial window, head post), non-aversive behavioural tests, whole body irradiation, EAE model which replicates multiple sclerosis