Vacation Scholarships May 2010

The first Medical Research Scotland Vacation Scholarships were awarded to the following, for the projects indicated:

William Bernard (Biomedical Sciences, Dundee University), to study the involvement of a particular protein in the control of intracellular sodium levels, under the supervision of Dr William Fuller.

The sodium pump is a cell membrane protein whose job is to transport sodium out of the cell: its activity is crucial for normal cell function. The sodium pump also plays a critical role in regulating the strength of heart muscle contraction. We have identified a protein (FXYD1) that provides the link between hormone stimulation and changes in sodium pump function. Evidence suggests that the FXYD1/sodium pump complex is defective in some forms of cardiovascular disease. The aim of this project is to investigate one of the mechanisms in cells that controls how FXYD1 regulates the sodium pump.

Roisin Brown (Medicinal Chemistry, Strathclyde University) for work investigating new methods to target delivery of anti-cancer drugs, under the supervision of Dr Nial Wheate.

Platinum-based drugs are one of the main families of chemotherapeutics. Whilst these drugs are useful in treating a large number of cancers, they are limited by severe side-effects. These side-effects arise from the indiscriminate attack of these drugs on all cells, both normal and cancerous. In this project we wish to develop a novel delivery vehicle for platinum drugs to completely remove the side-effects. This will involve the creation of iron nanoparticles that can be moved and directed in the body using magnetic fields. If successful, this project has the potential to increase both the likelihood of cancer treatment success as well as providing better quality of life to patients undergoing chemotherapy by removing all side-effects of platinum drugs.

Thomas Carson (Applied Pharmacology, Queen Margaret University Edinburgh), for a study of the interaction of resveratrol and oestradiol, the major form of the hormone oestrogen, under the supervision of Dr Iain Gow.

Red wine is known to give some protection against heart disease, probably by compounds known as phenolics which are found in red grapes. One of these compounds (resveratrol) is known to cause relaxation of isolated blood vessels and may act at targets (receptors) used by female sex hormones (oestrogens). This project aims to look at the interaction of resveratrol with oestradiol, the major human oestrogen. A better understanding of the mode of action of compounds such as resveratrol would highlight the importance of considering its interaction with oestrogen receptors throughout the body, especially for example in breast tissue.

Laura Castle (Medicine, Glasgow University), to work validating the use of cardiac MRI in the diagnosis of heart disease, under the supervision of Dr Colin Berry.

A magnetic resonance imaging (MRI) scan can reveal the nature of heart muscle damage in patients who have suffered a heart attack. For example, recent research suggests that MRI can reveal whether bleeding has occurred within the injured heart. This research aims to validate new MRI imaging methods by comparing scans of human hearts from cadavers, to the pathology seen after dissecting the hearts and viewing them microscopically. By determining the accuracy of MRI, this research may lead to new and more accurate clinical techniques being established to detect heart damage, thereby improving patient treatment.

David Clark (Medicine, St Andrews University), to study the role of the lymph cells in the rejection of kidney transplants, under the supervision of Dr Lorna Marson at Edinburgh University.

Kidney transplantation is becoming increasingly common, with 2,497 transplants having taken place in the UK last year. Transplants are performed in cases where the kidneys are no longer able to function sufficiently to keep the body alive, which can result from common conditions such as diabetes mellitus or hypertension. 5% of transplants fail annually due to rejection of the kidneys in the long term by the body; this research aims to determine whether the 'lymphatics' – a key component in the immune system – are involved in long-term rejection, as they may be a possible target for treatment of this condition.

Kirsty Farquharson (Medicine, Dundee University), to study the detailed effects of oestrogen on a cellular process pivotal in learning and memory, under the supervision of Dr Jenni Harvey.

Clinical studies have shown that cognitive performance in women declines during the menopause and with ageing. This deficit has been linked to reductions in the levels of the hormone, oestrogen. Recent studies have shown that oestrogen greatly influences learning and memory processes. Consequently, oestrogen-based therapies may prevent or reverse age-related decline in memory in women. However our understanding of how oestrogen influences brain function is limited.

Katia Hiersemenzel (Pharmacology, Edinburgh University), to investigate the regulation of the controlled death of white blood cells (neutrophils) in inflammation, under the supervision of Dr John Marwick.

White blood cells called neutrophils play a key role in protecting the body against invading organisms. The way in which neutrophils die is important as they contain toxic agents which would damage tissue if released in an uncontrolled manner which can contribute to the tissue damage associated with chronic inflammatory diseases. A new way by which neutrophils can kill invading organisms whilst dying, called 'netosis', has been discovered. We aim to understand if this new method of neutrophil cell death is harmful or beneficial in inflammation and, thereafter, if it may be manipulated by drugs as a therapy in disease.

Andrew Hutton (Immunology, Glasgow University), to investigate aspects of the immune system processes which result in bone destruction in rheumatoid arthritis, under the supervision of Dr Carl Goodyear.

Rheumatoid arthritis is associated with extensive bone erosion. The bone-eating cells (osteoclasts) responsible for this process, and the progenitor cells that they mature from, are found in greater numbers in the joints of rheumatoid arthritis patients. Therapeutic strategies that can target this aspect of the disease process are of intense interest. We have recently found that complexes, generated by mixing an endogenous human protein (immunoglobulin G) and a bacterial immunoglobulin-binding protein, have the ability to inhibit the maturation of osteoclasts. This project will examine this specific interaction and determine the ability of treated osteoclasts to remove bone.

Niklas Janisch (Microbiology/Genetics, Glasgow University), to work on a project investigating antibiotic-resistant forms of the bacterium *Pseudomonas aeruginosa*, under the supervision of Dr Daniel Walker.

Colonisation of the lungs of patients with cystic fibrosis by the bacterium *Pseudomonas aeruginosa* has been shown to be the main cause of mortality associated with this condition. The natural resistance of this pathogen to many commonly-used antibiotics and the acquisition of resistance to others can make *P. aeruginosa* infections very difficult to treat in some patients and there is an urgent need to develop new therapies. In people with cystic fibrosis *P. aeruginosa* can grow as a thin film in the lungs and in this state (biofilm) it is virtually impossible to eradicate with conventional antibiotics. Further, prolonged antimicrobial therapy leads to the development of highly resistant forms (known as small-colony variants) of the bacterium. The aim of this project is to test the ability of protein antibiotics (known as pyocins) to kill *P. aeruginosa* small-colony variants**.**

Lucy King (Genetics, Glasgow University), to study aspects of some defined mutants of strains of the bacterium E. coli O157, under the supervision of Dr Andrew Roe.

We are interested in new drugs to combat harmful bacteria. Our work has shown how these drugs might work, in that we now know what factors the drugs target. The project will work on bacteria that have had these target factors removed, thereby revealing what role they play for the bacteria. The project is central to our development of these new drugs.

Rohan Munir (Medicine, St Andrews University), to study the accuracy of current tests for predicting breast cancer subtypes, under the supervision of Dr Andrew Sims at Edinburgh University.

Breast cancer is a highly heterogeneous disease, determining the specific subtype is very important when selecting the most appropriate treatment. Research has been carried out over the past decade into the classification of breast cancer based on molecular subtypes in order to distinguish patients who will actually benefit from targeted therapies from those who will not, avoiding unnecessary treatment, side-effects and associated costs. However these new tests, one of which is currently being evaluated in a clinical trial, have recently been shown to be highly inconsistent. We will assess the accuracy of these tests on a larger scale, to determine the predictive value and robustness of these methods in determining the same molecular subtype.