Vacation Scholarships May 2011

19 Vacation Scholarships were awarded and the 17 accepted by the applicants for tenure during summer 2011 involve the following projects

Joanne Healy (Medicine, Aberdeen University), to study the potential of piracetam to protect mitochondria in sepsis and neropathy, under the supervision of Professor Helen Galley.

Some drugs used to treat cancer have the unpleasant side effect of severe nerve pain. There is some evidence that this pain might be caused by damage to a particular part of the cell, called mitochondria. This damage also occurs when patients have a severe infection (sepsis). Piracetam is a drug which is widely used for other conditions and which may be able to protect mitochondria. We can test whether such drugs can protect mitochondria, using cell models in the laboratory. This project will use existing cell models to test piracetam to see if it can protect cells against mitochondrial damage and whether it has potential future use in patients with nerve pain or sepsis.

Jay Hutchison (Microbiology, Aberdeen University), to study the role of protein-tyrosine phosphatase 1B (PTP1B) in the regulation of AMPK signalling, under the supervision of Dr Mirla Delibegovic.

PTP1B is a major regulator of glucose homeostasis and body weight through its role in insulin and leptin receptor pathways. Mice lacking the gene are resistant to the development of diabetes and obesity. AMPK is a protein which is activated during exercise and metformin, an anti-diabetic drug, exerts it effects by activating this protein. It is suggested that PTP1B may be able to regulate AMPK activity levels and maybe in this way improve insulin sensitivity. This project will test the hypothesis that deletion of PTP1B in fat cells will increase AMPK activitivity, by using a fat cell line which lacks PTP1B to investigate this in detail.

Euan Paterson (Human Biology, Queen Margaret University), for an investigation of the post-prandial effects of a meal rich in long-chain omega-3 fatty acids on indicators of cardiovascular risk, under the supervision of Dr Jane McKenzie

Evidence from population studies suggests that oily fish have a preventative role against the development of heart disease. Current recommendations indicate that we should consume two portions of fish per week, one of which should be oily, however intakes in Scotland are particularly low. The aim of this project is to investigate a link between the consumption of a meal containg oily fish and several factors indicating a potential reduction in the risk of heart disease. Understanding the immediate effects may help to provide more convincing evidence of how the regular consumption of oily fish may reduce an individual's risk of heart disease.

Imogen Bidwell (Medicine, Dundee University) for a study of estrogen and its therapeutic potential as a cognitive enhancer, under the supervision of Dr Jenni Harvey.

Clinical studies have found significant impairments in cognitive function in women following the menopause and with ageing. Decreased levels of the hormone estrogen have been linked to these deficits and recent studies have shown that estrogen markedly influences learning and memory processes. Thus estrogen-based therapies may help to alleviate cognitive decline in women. Our knowledge of how estrogen influences brain function is, however, limited. This project will investigate the effects of estrogen on a cellular event – AMPA receptor trafficking – that is key for learning and memory.

Karen Lai (Pharmacology, Strathclyde University) to investigate a novel treatment for glioblastomas using platinum-cucurbituril-based drugs, delivered in a nasal insert formulation, under the supervision of Dr Nial Wheate.

In this project we wish to develop a novel drug delivery system for the specific treatment of brain cancers. A dinuclear platinum drug (as a model for the clinical agent BBR3464) will be enclosed within a macrocycle called cucurbituril. This will then be formulated into nasal inserts, a novel method for delivering drugs that bypasses the blood-brain barrier. The performance of the nasal inserts will be examined to determine their drug release rates, solubility in simulated nasal fluid, stickiness to simulated muscosal membranes and their water absorption.

Dong Liu (Developmental Biology, Edinburgh University) to study nitrofuran activity in melanoma cells, under the supervision of Dr Liz Patton.

We aim to identify new drugs that may be effective for treating melanoma, the most lethal form of skin cancer with especially high incidence in Scotland. Nitrofurans are potent drugs used to treat bacterial and trypanosome infections, and more recently have been shown to treat brain cancers. Nitrofurans have been found to be able to kill melanoma cells and also melanocytes, the pigment cells that can become melanoma. This project aims to identify melanoma cells that are sensitive to nitrofurans.

Agnieszka Rybacka (Biomedical Sciences, Dundee University) to investigate the effect of short-term, high-fat feeding on cognition, under the supervisio of Dr Caroline Stewart.

Dementia is a progressive and debilitating disease which costs more to manage than heart disease, stroke and cancer combined. Risk increases with a diagnosis of type 2 diabetes and obesity; both of which are now at pandemic levels. An understanding of why these factors increase dementia may help establish interventions to treat individuals before irreversible damage occurs. This study will use an animal model to examine why relatively short periods on a high-fat diet seem to affect certain types of learning. Results may suggest lifestyle changes or treatments which could reduce the increase in dementia associated with poor diet.

Huma Yousuf (Human Biology, Queen Margaret University) to study the effect of 17-beta oestradiol on Na+/H+ exchange in breast cancer cell lines, under the supervision of Dr Iain Gow.

The tumour environment is more acidic than normal (*p*H 6.8 *vs* 7.3), and this may aid tumour progression or affect the uptake of drugs. The extracellular *p*H may, be part-regulated by cellular sodium/hydrogen exchangers (NHEs), and NHE activation may, in turn, be regulated by hormones such as oestradiol. Some breast cancers have oestradiol receptors and stimulation or blockade of these may modulate the cell's ability to regulate *p*H. This project will investigate the effect of oestradiol on the ability of breast cancer cells grown in the laboratory to regulate their *p*H by NHE.

Anjali Gangadharan (Medicine, Edinburgh University) to investigate the relationshp between capillary development and disease progression in a mouse model of spinal muscular atrophy, under the supervision of Dr Simon Parson.

Spinal Muscular Atrophy (SMA) is a common, inherited form of motor neurone disease. These conditions affect the specialised nerve cells in the spinal cord which control our every movement. The first signs of damage as the disease progresses are found in the connections between nerve cells and muscle and it is suggested thtat the blood supply to these muscles may also be compromised. This project aims to measure the extent of blood vessel development in diseased muscles and determine if changes in blood supply cause, or are a consequence of, disease progression.

Joshua Newmark (Medicine, St Andrews University) to study sex differences in the cytoarchitecture of the midbrain dopamine system, under the supervision of Dr Gillian Brown.

Parkinson's disease is a neurological disorder that involves progressive loss of dopamine-producing cells in the midbrain. Clinical studies have shown that men are approximately one-and-a-half times more likely to suffer from Parkinson's disease than women, but the reasons for this sex difference are not well understood. This project will examine the midbrain dopamine systems of male and female rodents at adolescence and adulthood, aiming to identify possible explanations why men are more susceptible to Parkinson's than women and possibly direct future drug development.

Catriona Neil (Medicine, Dundee University) to study phototoxicity and photoallergy of non-steroidal anti-inflammatory drugs, under the supervision of Dr Julie-Ann Woods.

Sometimes medicines we take can react with sunlight to produce reactions in our skin. Such medicines include pain-relieving anti-inflammatory drugs such as Ibuprofen and some patients develop a life-long allergy as a result. To find out if a patient has developed a photocontact allergy to a medicine, we carry out a photopatch test on them. This is nor a perfect method, however and can generate a false positive result. The aim of our project is to better understand how we can distinguish between a false positive and a real result.

Eric Cruickshank (Immunology, Glasgow University) to investigate the epigenetic regulation of osteoclast differentiation, under the supervision of Dr Carl Goodyear.

Bone ersoion is a feature of many diseases including rheumatoid arthritis, osteoporosis and multiple myeloma. The bone-eating cells (osteoclasts) responsible for this process, and the cells from which they mature, are found in greater numbers in the diseased condition. Strategies that can target this aspect of the disease process are of intense interest. Recently, a therapeutic has been found that can manipulate this process through the regulation of the genetic material that controls the fate of the precursors of osteoclasts. This project will examine the mechanisms underlying this regulation.

Emma Joseph (Human Embryology & Developmental Biology, Aberdeen University) to investigate the role of a completely novel serine/theornine kinase in neurite outgrowth, under the supervision of Dr Bing Lang.

Schizophrenia is associated with multiple genetic factors. It is known that a novel serine/threonine kinase (STK) is deleted in schizophrenia patients, highly expressed in neuropathological sites and binds DISC1, the strongest genetic factor in schizophrenia. Neurites are critical for brain cell communication. Neuroblastoma cells lacking STK grow fewer and shorter neurites. This project will add STK cDNA, or a control vector, to the modified cells lacking STK, anticipating that by 'forcing' STK expression, the defectiveness in the modified cells will be corrected, thus further supporting the hypothesis that appropriate STK expression is critical for brain cell communication.

Faith Dalgaty (Medicine, Dundee University) to investigate the pharmacology and cellular expression of GPR92, a novel lipid-sensing receptor, under the supervision of Dr Andrew Irving.

GPR92 is a cell protein found in the membrane of cells that communicate pain to the brain, so that we are aware that we feel pain. It is also found in cells involved in inflammation. It is thought that GPR92 is involved in the process of registering the pain associated with inflammatory conditions such as Multiple Sclerosis and infectious injury inflammation. This project will investigate how the protein sends signals within the cell, improving understanding of the communication between the inflammation site and the pain felt. The results may point to future drug development to block the process.

Siobhan Hoy (Pharmacology, Glasgow University) to study levels of apoptosis following cerebral ischaema, under the supervision of Dr Rachel Shirley.

Stroke is the 3rd leading cause of death in the UK and the major cause of long-term disability. There is an urgent need to find new intervention strategies, as there is currently only one approved therapeutic. Stroke results in the activation of many biochemical pathways, leading to brain cell death. This project aims to assess how effective targeting two of these pathways are at improving outcome. It will investigate the effects of using a modified cell-death (apoptosis)-promoting gene triggered by stroke and also a drug to lower levels of the oxidative stress associated with stroke. The results could have important implications for future interventions in the clinic.

Vojtech Prazak (Medical Microbiology, Aberdeen University) to carry out structure-function studies of critical gating residues in mechanosensitive channels, under the supervision of Dr Samantha Miller.

Channels are specialised molecules which are essential for all cells to grow. The mechanosensitive channels are involved in pain, touch, hearing and balance. In bacterial cells they are required for cells to survive water stress and are thus a potential new target for antimicrobial therapies. This project will use modern molecular and genetic techniques to identify regions of the mechanosensitive channels that are essential for their function and thus inform our ultimate goal to provide novel strategies to combat bacterial infections.

Marta Wylot (Sports & Exercise Science, Aberdeen University) to investigate whether inhibition of mitochondrial citrate synthase be used in prevention of obesity, under the supervision of Dr Aivaras Ratkevicius.

Obesity and diabetes are associated with abnormal utilisation of nutrients by the body. This is often due to poor function of the mitochondria, the 'energy factories' of the cells. It is suggested that resistance to obesity in some mice could be due to a particular mutation in the gene coding for the mitochondrial citrate synthase (CS). This projects will investigate how this particular mutation of the gene changes citrate synthase as an enzyme, with the aim of clarifying its potential future use as a target for the treatment of obesity.