Vacation Scholarships 2014

Thirty-five applications were submitted and a total of 30 awards were finally accepted. The host universities are distributed as follows: Aberdeen (2); Dundee (3); Edinburgh (9); Glasgow (11); Queen Margaret (1); St Andrews (4).

Anonymous [Human Biology] & Dr Iain Gow, Division of DNBS, Physiotherapy, Podiatry, and Radiography, Queen Margaret University
Endothelial function during an oral glucose tolerance test in young, healthy volunteers
The heart and blood vessels of the body can become damaged over time leading to disease, though causes of this damage are not fully understood. High levels of blood sugar are associated with damage, and this has been seen in older people with diabetes or high blood pressure. It is not clear if this happens in younger people (i.e. under 50 years) which may indicate that damage occurs early in life. We propose giving young volunteers drinks containing either sugar or artificial sweetener, and measuring blood sugar, and blood vessel "health" in a similar way to taking blood pressure.

Deimante Barkauskaite [Pharmacology] & Dr Ian Salt, Institute of Cardiovascular & Medical Sciences Glasgow University
Regulation of mitogen-activated protein kinase (MAPK) activity by AMP-activated protein kinase (AMPK) in endothelial cells
Atherosclerosis (narrowing or "furring up" of the arteries) is the main cause of heart disease and stroke. In healthy people, the cells that line blood vessels (endothelial cells) maintain cardiovascular health yet this beneficial action is lost in response to a variety of factors, such as high blood pressure, obesity and diabetes. We have previously shown that a protein called "AMPK" can block this switch from a healthy to diseased endothelium. Furthermore, we have shown that AMPK reduces the activity of important cellular proteins called "MAPKs" which are activated in the early stages of atherosclerosis by a mechanism that is currently unknown. This proposal seeks to understand the mechanisms by which AMPK inhibits MAPKs in human endothelial cells cultured in the laboratory. By identifying processes that limit MAPK activation in the endothelium, we will not only determine how AMPK activation may limit cardiovascular disease but may also identify new targets for more effective drugs.

Helena Brewer [Veterinary Medicine & Surgery] & Dr Jayne Hope, Infection & Immunity, Roslin Institute, Edinburgh University
Identification of key cytokines and cell populations driving gut inflammation in cattle with Johne's disease
Johne's disease (JD) is a chronic gut disease which affects a large number of animals causing significant economic and animal welfare concerns. In order to design effective vaccines to prevent disease we must first understand the changes that occur within infected animals. We propose to study the cells that are associated with the inflammation that is seen in the gut. There are established links between JD in cattle and Crohn's disease in humans. Both Crohn's disease and JD have chronic inflammation in the gut and parallels can be drawn from studies in cattle to aid understanding of human disease.

Gavin Chapman [Medicine] & Professor Adriano Rossi, Centre for Inflammation Research, Edinburgh University
Investigating neutrophil formyl peptide receptor number and function in bronchiectasis
Bronchiectasis is a chronic lung disease that results in frequent infections leading to repeated courses of antibiotics, hospital admissions and in many cases an early death. One of the hallmarks is accumulation of white blood cells in the lung, these cells are useful in fighting infection but too many of them results in worsening lung damage. The white cells are drawn in by recognising specific factors released in the disease process. Investigating the role these factors play, and how they interact with and influence white cell function, will improve understanding of bronchiectasis and potentially aid the development of new and better drugs. In this project we will take blood from bronchiectasis patients and measure the presence of one specific recognition protein used by white cells to navigate into the lung and then look to see whether the bronchiectasis white cells respond differently. This project will help determine whether this protein is a potential drug target.

Chelsea Cook [Pharmacology] & Professor Roger Pertwee, School of Medical Sciences, Aberdeen University
A search for novel positive and negative allosteric modulators of the cannabinoid CB1 receptor
Cannabinoid CB1 and CB2 receptors, and endogenously-produced compounds (“endocannabinoids”) that activate these receptors, constitute the “endocannabinoid system”. Research, here and elsewhere, has shown that the potency and/or maximum ability of drugs to activate CB1 receptors can be enhanced or inhibited by targeting “allosteric” sites on these receptors. This project would explore the ability of novel compounds to behave in vitro as allosteric CB1 receptor enhancers or inhibitors. Such compounds could well constitute important new medicines, since endocannabinoids are released onto CB1 receptors in certain disorders, in a manner that appears to ameliorate (e.g. multiple sclerosis), or exacerbate them (e.g. obesity).

Emanuel Ferreira Lopes [Neuroscience] & Dr Andrew Irving, Division of Neuroscience, Dundee University
The prokineticin system as an emergent modulator of neuronal function
Receptors that sense endogenous peptides are important in norman brain function and in human disase. The project aims to investigate the properties of a new family of peptide receptors at the cellular level. The investigation of these receptors is significant as current research has suggested that they may have a role in the signalling pathways involved in pain and neurodegeneration.

Teodora Filipescu [Medical Sciences] & Dr John Lucocq, Department of Medicine, St Andrews University
Identification and localisation of phosphoinositide lipids in intracellular microsporidian parasites using novel quantitative electron microscopic affinity methods
A major portion of human beings are infected with parasites called microporidia that live inside our gut cells. They are implicated in increasing the mutation rate and potentially increasing the risk of cancer. They are also important causes of disease when the immune system is weakened as in AIDS. The genome of these organisms predicts proteins that synthesise important membrane lipids called phosphoinositides. We will find out if and where in the cell these lipids are made using sensitive electron microscope techniques. By identifying the phosphoinositide types, the proteins that make them will become potential drug targets against these organisms.

Anna Francis [Medical Sciences at Durham University] & Dr Neil Henderson, Centre for Inflammation Research, Edinburgh University
Investigation of the role of hepatic stellate cells during liver carcinogenesis
Liver cancer is the commonest cause of death in patients with cirrhosis (severe liver scarring), and is resistant to most chemotherapy. Most tumours occur in cirrhotic livers, but the mechanisms linking cirrhosis and cancer are poorly understood. The hepatic stellate cell is the major source of scar tissue during liver injury, and we will investigate the role of this cell in hepatocarcinogenesis. Furthermore, using a mouse model of liver cancer, we will assess the effect of removing a protein (αv integrin) specifically on stellate cells, to investigate its role during hepatocarcinogenesis. This will hopefully identify novel chemotherapeutic targets resulting in better treatments for patients with liver cancer.

Jennifer Hayden [Biochemistry] & Dr Marie Freel, Institute of Cardiovascular & Medical Sciences, Glasgow University
The role of microRNAs in the regulation of adrenal aldosterone production.
Increases in the production of the steroid hormone aldosterone is important in patients with high blood pressure and other cardiovascular disorders. These increases may be due to abnormalities in the mechanisms which regulate its production . We wish to examine whether its production is regulated by a new class of small molecules called microRNAs. This will help us determine how aldosterone production is regulated and identify new targets which could be manipulated to lower the levels of aldosterone production and develop new approaches to the treatment of cardiovascular disorders.

Angela Hu [Medicine] & Dr Melissa Andrews, Anatomy, St Andrews University
Evaluation of cell-specific promoters to target different motor-neuron subtypes
Spinal cord injuries are very prevalent in our current society, and are highly debilitatating to the patient involved. As of yet, there are no definitive treatments for this condition due to the difficulty of regenerating cells in the nervous sytem, called neurons. In this project, we will examine specific promoters which target gene expression in certain neuronal subtypes, particularly gamma motor neurons (the neurons involved in muscle contraction). These experiments will involve construction of appropriate plasmids (small pieces of transferable DNA), transfection of the constructed plasmid into a suitable cell line, and analysis of expression of a gene of interest.

Rebecca Hughes [Biochemistry] & Dr Silvia Paracchini, School of Medicine, St Andrews University
Functional investigation of the PCSK6 genetic variants associated with laterality: implications for neurodevelopmental disorders
Dyslexia is a specific impairment in reading ability, affecting 10% school-children. It has a strong genetic component, still largely unknown. For a long time a link between handedness and dyslexia has been proposed. Recently, we have identified the first gene (PCSK6) to be robustly associated with handedness, specifically in children with dyslexia. PCSK6 is known to control left-right body asymmetries. It has been shown that dyslexia candidate genes are implicated in related pathways.
We will study the functional mechanisms underlying the PCSK6 association to further understand the biology of handedness and dyslexia. The results may have important implications for dyslexia diagnosis and intervention.

Jee Soo Kim [Medical sciences] & Dr Tara Spires-Jones, Centre for Cognitive & Neural Systems, Edinburgh University
Interactions of amyloid beta and tau in a new model of Azlheimer's Disease
Alzheimer's disease is a devastating neurological disorder that affects millions of people. Currently, we do not have effective treatments for Alzheimer's. The goal of this project is to determine whether the two molecules that accumulate in the brain of Alzheimer's sufferers (called amyloid beta and tau) interact to cause the death of brain cells and the connections between cells. The student will count brain cells and pathological lesions in a new model of Alzheimer's. These studies will help direct research in developing treatments.

Nils Korte [Physiology] & Professor Keith Muir, Institute of Neuroscience & Psychology, Glasgow University
Serial MR Spectroscopy Assessment in the PISCES Phase 1 Clinical Trial of Human Neural Stem Cell Implantation in Ischaemic Stroke
Stroke affects 150,000 people annually in the UK. Loss of brain tissue leaves more than half of survivors with some permanent disability, but we lack treatments that can improve recovery. Stem cells are a promising means of stimulating tissue repair. The PISCES trial was a "first in man" safety study of neural stem cells in people after stroke. The study involved detailed brain scans in all participants before and after cell implantation, and this project will involve analysis of these scans to investigate whether any changes in brain chemistry are seen, and how these relate to clinical progress.

Yen Lau [Medicine] & Dr Paul Reynolds, School of Medicine, St Andrews University
Investigating gemcitabine resistance in pancreatic cancer
There is a growing need to personalise anti-cancer treatments because cancers, like individuals, are somewhat unique. Diagnostic assays detecting specific features (biomarkers) provide a framework to classify tumours according to their molecular content. In turn, the specific cancer profile guides the clinician's choice for therapy. This personalised medicine approach will markedly increase the effectiveness of cancer treatments. Although gemcitabine is the backbone of several cancer treatments, it is effective in only the minority of patients; major resistance mechanisms in cancer cells dramatically limit its activity. Hence, patients receiving this compound have only a marginally improved life-span, compared with untreated individuals. This project will characterize conditions in pancreatic cancer cells in which there is an effect on the levels of drug resistance to gemcitabine.

Puay Lee [Medical Sciences] & Dr Steven Pollard, MRC Centre for Regnerative Medicine, Edinburgh University
Is FoxG1 expression activated in midbrain and hindbrain neural stem cells when they are expanded *in vitro*?
Brain tumours are driven by cells that display characteristics of neural stem and progenitor cells. The Pollard laboratory is studying how gene regulatory processes that are used during development in the construction of the forebrain operate in adult brain cancer. This project will assess whether the forebrain specific transcription factor FOXG1 is activated when midbrain and hindbrain stem cells are cultured *in vitro*. FOXG1 may be important in providing susceptibility to transformation of normal cells into brain cancer cells. Therefore if we can expand FOXG1 negative midbrain and hindbrain derived neural stem cells, then we can in the future test directly whether FOXG1 is a critical factor underlying brain tumour susceptibility.

Phoebe Makiello [Medicine] & Mr Ian Currie, Surgery, University of Edinburgh
Hepatic Encephalopathy in Liver Transplant Candidates
Hepatic Encephalopathy is a potentially fatal complication of advanced liver disease. This condition is thought to occur when blood draining from the gut, containing toxic metabolites, is able to bypass the liver and affect the brain. In liver patients, large bypass channels may form which contribute to this pathophysiological shunting. Once formed, these channels decompress the high blood pressure in the veins, a key indicator of which is a reduction in the size of the spleen. We hypothesise that spleen size, easily measured by simple ultrasound, is inversely related to the risk of encephalopathy in liver disease. The project will assess spleen size and the relationship with intra-abdominal venous shunts and encephalopathy in patients with liver disease. The objective is to derive a risk score which will help non-specialists identify those patients at higher risk of encephalopathy before the development of this life-threatening complication.

Sarah McGrath [Immunology] & Dr Carl Goodyear, Institute of Infection, Immunity & Inflammation, Glasgow University
The effect of cytokine blockade on rheumatoid arthritis synovial fluid stimulated macrophage.
Inflammation of the joints is one of the main clinical characteristics of rheumatoid arthritis. In non-diseased situations the joints are bathed in synovial fluid, which contributes to the health of joints. However, in rheumatoid arthritis the composition of the synovial fluid is dramatically changed and thus drives the disease process. Newly emerging therapies target components within the synovial fluid, which are known to stimulate immune cells that have moved into the joints. The proposed studies in this project will examine one of these therapies to understand how it can alter the stimulation of our immune cells. This will hopefully give us insight into aspect of the disease process and how therapies alter this.

Kathryn Pennel [Immunology] & Dr Shauna Culshaw, Infection & Immunity, Glasgow University NETting' Bacterial Biofilms - Do neutrophils generate extracellular traps to combat bacterial biofilms?
In response to infection specific immune cells called neutrophils are known to kill bacteria in a number of ways. One of these killing mechanisms is through production of structures called Neutrophil Extracellular Traps or 'NETS'. This type of killing helps clear bacterial infections but molecules associated with these NETS play a role in immune system malfunction which causes damage to self as well as bacteria. A particular enzyme essential for NET formation, called PADIV, is associated with rheumatoid arthritis which is a common and devastating disease in which the immune system attacks the joints. The aim of this project is to investigate how NETS impact on different types of bacteria. This should result in a better understanding of how the immune system deals with bacterial infections and the role of infections in autoimmunity.

Alexander Petric-Gray [Neuroscience] & Professor Frank Pollick, Psychology, Glasgow University
Development of a functional Magnetic Resonance Imaging (fMRI) system for neurofeedback
In many forms of therapy it has been shown to benefit patients to provide useful feedback of their performance. For conditions related to cognitive and mental activity providing feedback has previously proven challenging due to inability to measure and interpret brain activity. However, with recent advances in brain science and computing it is now possible to reliably obtain measures of brain activity related to particular cognitive states and provide feedback. We are currently developing such a neurofeedback system using fMRI, ultimately for use in pain therapy, and the student will assist in this development.

Fiona Plain [Pharmacology] & Dr Sheriar Hormuzdi, Division of Neuroscience, Dundee University
Investigating the importance of KCC2 phosphorylation in regulating Chloride extrusion
The protein, potassium-chloride cotransporter (KCC2) is found in neurons and ensures that specialized chemical channels in brain cells will be activated. This activation is important for allowing the brian to function properly since neuropathic pain and specific forms of epilepsy can occur if the transporter is deficient. Despite its importance there are many aspects about the function and control of the transporter that we do not know. This project will examine the hypothesis that phosphorylation, a form of protein modification, can regulate the function of KCC2. The experiments will introduce mutated versions of KCC2 in cells and use a specialized microscope to probe living cells. Our results will determine whether phosphorylation may be a means to enhance or diminish KCC2 function with implications for treating pain and epilepsy.

Susana Qasem [Physiology] & Professor Trevor Stone, Institute of Neuroscience, Glasgow University
Regulation of neuronal growth by tryptophan metabolites
We have found that a group of compounds generated from the amino acid tryptophan affect the early development of the brain in embryos. This project will use cell cultures to explore the mechanisms of this. Nerve cells will be cultured and exposed to five of the major kynurenine metabolites for at least 24h, after which the candidate will determine cell growth, proliferation rate and ability of the cells to follow molecular guidance cues and form connections. The results will add greatly to understanding factors that affect the earliest stages of brain formation.

Sonia Rehman [Medical Sciences] & Dr Christopher Mowat, School of Chemistry, University of Edinburgh
Development of a High-Throughput Screen for Specific Inhibitors of Human Indoleamine Dioxygenase-2
Three related proteins are believed to play a role in cancer development in humans, helping the tumour to evade the body's immune response. These are TDO (tryptophan 2,3-dioxygenase), IDO1 (indoleamine 2,3-dioxygenase-1) and IDO2 (indoleamine 2,3-dioxygenase-2). Several inhibitors (potential chemotherapy drugs) of IDO1 and TDO have been identified. However, the specific roles of the enzymes in cancer are still unclear. To better understand the role of IDO2 it will be advantageous to obtain specific inhibitors of the enzyme. This project seeks to determine conditions under which it is possible to rapidly test compounds as IDO2 inhibitors for further characterization.

Sona Relovska [Reproductive Biology] & Professor Philippa Saunders, MRC Centre for Reproductive Biology, Edinburgh University
Investigations into the association between endometriosis and natural killer cells
Endometriosis occurs when the lining of the womb (the endometrium) grows outside the womb, usually on the lining of the body cavity resulting in debilitating pelvic pain and infertility. The tissue fragments attract immune cells including natural killer (NK) cells. NK cells have the ability to kill other inappropriate cells present in the body. It is thought that NK cells might not function correctly in women with endometriosis, meaning that endometriosis cells are not killed and this may explain why they persist and grow. The aim of this project is to visualise NK cells in samples of endometriosis tissue from women and mice so we can learn more about their function and role in this disease.

Ana-Maria Ristoiu [Neuroscience] & Dr Jenni Harvey, Division of Neuroscience, Dundee University
Evaluation of the potential use of leptin mimetics in the treatment of neurodegenerative disease
Clinical studies have identified a link between leptin levels and the incidence of Alzheimer's disease (AD). Leptin is also neuroprotective in rodent models of AD. Thus leptin-based therapies may be beneficial in AD, but leptin treatment may not be the best approach due to its widespread actions. However, different parts of the leptin molecule are responsible for its diverse biological actions. Thus development of small peptides that mimic the brain actions of leptin is a novel therapeutic strategy. In this study we propose to identify the region/s of the leptin molecule responsible for its anti-AD properties using electrophysiological approaches.

Ana Rondelli [Neuroscience] & Professor Andrew Jarman, Centre for Integrative Physiology, Edinburgh University

Using CRISPR technology to investigate the function of primary ciliary dyskinesia candidate genes in the fruit fly, *Drosophila*

Primary ciliary dyskinesia (PCD) is an inherited condition affecting the lungs and fertility. It is most prevalent in ethnic communities. It is necessary to identify the faulty genes that can cause PCD. A number of 'candidate' genes have been suggested from animal studies including, perhaps surprisingly, the fruit fly. This insect is commonly used for investigating fundamental aspects of disease mechanisms due to its ease of laboratory culture and genetic analysis. The student aims to characterise the roles of two such candidate PCD-causing genes in the fruit fly. She will mutate the genes (thereby mimicking the PCD condition) and look for the effects on the physiology of the flies. This information will be used in the future to guide human PCD research.

Amy Taylor [Anatomy] & Professor Godfrey Smith, Cardiovascular and Medical Sciences, Glasgow University

The effects of prolonged period of high beating rates on iPS derived heart cells

The purpose of this project is to measure the effects of prolonged periods (4-5 days) of high heart rates on the electrical and mechanical properties of human heart cells derived from induced pluripotent stem cells. In adult humans long periods of high heart rates (tachycardia) can induce a form of heart failure even if normal heart rate is restored. The heart cells enlarge and the contractility decreases as a result of the prolonged periods of taxhycardia. The mechanisms underlying this phenomon are poorly understood because of the lack of suitable experimental models. This project will investigate whether this form of cardiac dysfunction can be induced in a human heart cell line. If dysfunction is caused by this protocol, this model could be used to investigate cause and treaments for this condition.

Yue Teng [Medicine] & Professor Colin Berry, Institute of Cardiovascular & Medical Sciences, Glasgow University

In heart attack survivors, are coronary artery plaque characteristics associated with the risk of more heart injury in the future?

Heart attack survivors who have more than one narrowed heart artery are at a particularly increased risk of another heart attack in the future. In the Golden Jubilee National Hospital in Glasgow, have recently completed recruitment of one of the largest 'heart attack' studies with 324 heart attack patients, all of whom had detailed heart artery imaging and longer term follow-up. Since all of the scans have been collected, we now wish to study the nature of the heart artery narrowings in more detail in order to better understand the plaque characteristics (shape, irregularity etc) which are associated with patients who have had a further heart attack. In the future, the information from this project could help doctors to identify patients who may or may not be at risk of another heart attack.

Jessica To [Physiology] & Dr Dilys Freeman, Institute of Cardiovascular & Medical Sciences, Glasgow University

High density lipoprotein function in pregnancy

Maternal obesity is common and carries an increased risk of adverse pregnancy outcome. In healthy pregnancy the mother's blood vessel function increases to allow an adequate blood supply to the placenta thus providing oxygen and nutrients for the baby. A particle in the blood, high density lipoprotein (HDL), is known to protect blood vessels walls from oxidative stress and when HDL concentrations are low, poor vessel function and cardiovascular disease develops. The role of HDL in the improvement in blood vessel function in pregnancy and how it is changed in vascular diseases of pregnancy such as preeclampsia is not known.

Natasha Walker [Biomedical Sciences] & Dr Nicola Mutch, Institute of Medical Sciences, Aberdeen University

The janus face of FXII - a potential role in coagulation and fibrinolysis

Recent work has shown that the protein factor XII is involved in blood clot formation within vessels, but not in stopping bleeding after injury. Our work identified polyphosphate, a component of platelets, as the first 'natural' activator of factor XII. Preliminary work suggests factor XII can act both in the formation and breakdown of clots. This project will investigate the ability of polyphosphate to regulate the function of factor XII in breaking down blood clots. The ultimate goal of our studies is to develop a better understanding on how to treat individuals at risk of strokes or heart attacks.

Ellanor Whiteley [Biochemistry] & Dr Timothy Palmer, Institute of Cardovascular & Medical Sciences, Glasgow University

Detecting Serine 515,518-phosphorylated JAK1, a novel mechanism for the anti-inflammatory effects of AMP-activated protein kinase (AMPK)

If unchecked, defective functioning of so-called “endothelial cells” (ECs) that line blood vessels results in cardiovascular disease. For example, the narrowing of the arteries responsible for heart disease is caused by chemicals called "cytokines" which trigger an inflammatory response in ECs by activating a critical intracellular "JAK-STAT" pathway. This then turns-on genes responsible for inflammation and defective function. Our studies have identified a process by which a protein called “AMPK” directly inhibits one of the JAKs. By examining how this pathway works, the student will help us evaluate its usefulness as a target for reducing inflammation in cardiovascular disease.

personalised tumour treatment.