STUDENT ABSTRACTS

In line with the symposium theme of Societal Impact, students were asked to submit lay abstracts of their research projects.

These abstracts should be accessible to all audiences of different backgrounds, giving detail and emphasis on the impact the research will, or could potentially have, on society.

Please vote for the student from each cohort who you think submitted the best abstract conveying Societal Impact in their project, by following the link below.

https://www.surveymonkey.co.uk/r/F5BG5HL

1ST YEAR STUDENTS

Mimi Asogwa, University of Aberdeen.
Investigating the role of mechanosensitive channel YnaI in Salmonella pathogenesis.
Dr Sam Miller, Dr Stefania Spano and Dr Mark Stevens.

Salmonella enterica is a food-borne pathogen that affects humans worldwide, causing about 27 million cases of typhoid fever and 100 million cases of gastroenteritis annually. Salmonella enterica also affects other hosts such as farm animals, where they act as key reservoirs of infection. In farm animals, Salmonella cause salmonellosis, a disease which affects productivity and have public health implications. However, the mechanisms by which Salmonella colonise their hosts and cause disease require further study.

Mechanosensitive channels are required for bacterial cells to survive hypoosmotic shock (transition from high to low salt environment). YnaI is a mechanosensitive channel found amongst many bacterial species including Salmonella. Recent studies have suggested that YnaI is required for host colonization and/or pathogenesis during bacterial infections of farmed animals. Disruption of YnaI in Salmonella impaired intestinal colonization in pigs, cattle and chicken; while in Campylobacter jejuni, a closely related protein was required for colonization in chicks.

YnaI exhibits unique characteristics but its structure and mechanism of channel opening are not well understood. My project aims to understand YnaI structure and function, to ascertain key domains required for YnaI channel opening. I will further investigate the role of YnaI during Salmonella infection of animals to determine if YnaI is required for processes such invasion and replication. Understanding the role of YnaI in Salmonella infections will enhance understanding of mechanisms used by Salmonella in hosts colonization and disease. It will also provide opportunity to create new strategies to reduce food contamination and ultimately the incidence of food-borne infections in humans.

Fiona Bakke, University of Aberdeen.
From sharks to humans: enhancing our understanding of immunity.
Dr Helen Dooley, Dr Dan Macqueen, Dr David Stead.

Sharks evolved approximately 450 million years ago, and were the first animals to have an immune system similar to ours, if somewhat more basic (think Model T Ford compared to a Ferrari). However, the fact that sharks still exist means they are capable of defending themselves against both ancient and recent diseases, so we believe we can learn a lot from these ancient animals.

New technologies allow us to examine more closely the proteins which sharks use to fight infection and to compare these to proteins which humans and other animals use. We are therefore investigating the immune systems of sharks as well as animals which evolved more recently, such as bony fish (eg, rainbow trout), amphibians and reptiles, to see which immune proteins changed, were gained, or were lost, as these new groups of animals evolved. We are interested in tracking these evolutionary changes, because investigating even tiny changes in these proteins may help us identify new targets to help us develop medicines to treat auto-immune diseases which affect humans, such as rheumatoid arthritis, Crohn's disease, multiple sclerosis, Type I diabetes and psoriasis. These occur when the body's immune system detects normal tissues but misidentifies them as abnormal and mounts an immune defence against them, resulting in damaging effects.

Assembling a complete evolutionary picture of the development of the immune system will enable us to identify which changes in the immune proteins implicated in these diseases occurred, which will then help us to develop ways to combat these diseases.

1ST YEAR STUDENTS

Rosie Barraclough, University of Edinburgh.
Use of advanced technologies to enhance monitoring of dairy cow health.
Marie Haskell, Robert Boyce, Alastair Macrae.

In the last twenty years, the average number of cows in UK dairy herds has doubled to 143 cows, resulting in reduced individual cow attention and less time for stockmen to detect health issues. There is therefore a requirement to develop systems to automatically detect disease. Lameness and mastitis are common production diseases of dairy cows, resulting in a combined yearly economic loss of £325 million for the UK dairy industry and reduced animal welfare.

Changes in cow behaviour can be indicative of disease, and the collection and analysis of behavioural data could potentially be used for real-time decision making by stockmen to detect cow health issues.

IceRobotics (Edinburgh, UK) have developed CowAlert®, an automated non-invasive behavioural monitoring system for dairy cows, which uses tri-axial accelerometers (IceQubes®) to measure behavioural activity. The system is predominately used for heat detection, but could be developed further to monitor cow health. The study will use IceQubes® to measure the behaviour of 100 dairy cows to determine if cow behaviour alone, or in combination with production parameters, can detect specific disease conditions. The study will also determine if cow behaviour can be used as an alert system to predict calving and health issues relating to calving.

Data driven biology has the potential to redefine and improve farm management practices, essential for achieving sustainable agriculture and food security. Cow health and welfare is important to consumers, and objective assessments of disease will improve public perception and maintain trust in the UK dairy industry.

Christina Brown, University of Edinburgh.
Exploration of the neuronal circuits within the lateral entorhinal cortex.
Professor Matthew Nolan, Dr James Ainge.

Episodic memories involve the remembrance of places, people and events, which may also be combined to processes like emotional attachment. How we can link all the information needed to remember an ‘episode’ in our lives in such a complex manner is a defining feature of being human. One of the brain areas thought to be heavily involved in doing this is the lateral entorhinal cortex (LEC). Despite its importance, little is known of the LEC’s connection to other brain areas and how its cell populations contribute to memory processes.

I plan to apply specific molecular tools that were developed for another part of the brain – the medial entorhinal cortex – onto specific cell populations and pathways in the LEC. The results from these studies will not only help us understand how complex, layered episodic memories are formed but can also be helpful in understanding Alzheimer’s disease. Alzheimer’s disease is characterised by memory loss, followed by confusion and problems with speech and understanding. Alzheimer’s disease affects 62% of the 850,000 dementia sufferers in the UK but there are no effective treatments. The disease has massive societal and financial implications in the UK, with an ageing population and cost of social care increasing exponentially. Alzheimer’s disease spreads outwards from the entorhinal cortex, which means more in depth analysis of the LEC can be applied towards drug target therapies before the onset of observable symptoms.

1ST YEAR STUDENTS

Max Brown, University of Edinburgh.
The origin of hybrid species in Euphrasia L.
Dr Alex Twyford, Dr Gail Jackson.

You may have heard of carnivorous plants but have you ever heard of parasitic plants?

There is a whole world of plant species who need to parasitise other plants to ensure they survive. These plants can have a huge effect on ecosystems around the world and in turn, they represent a major threat to crop yields worldwide. A relative of the damaging pest species is a genus called Euphrasia which could help shed light on the origins and maintenance of parasitism. Euphrasia is a complex group of species because they hybridise very readily with other species of Euphrasia. Hybridisation is where one species interbreeds with another, forming individuals that are generally intermediate in their characters. Some hybrid individuals are able to become isolated from either of the parents and may eventually form a distinct new species. The most important factors in so called hybrid speciation are reproductive isolation and hybrid fitness. In order to investigate this further, I have started to grow and cultivate thousands of plants, which will enable me to look at the differences in fitness that different hosts have for a single species of Euphrasia. This will be taken further to understand the fitness differences of different species of Euphrasia (hybrids and parents) on the same suite of hosts. Lastly I will sequence the DNA of the hybrid species and the parents to look at how the genomes have changed over time, a mechanism for hybridisation and in time a better understanding of the evolution of these plants. Our understanding may lead to breakthroughs in controlling pest parasitic plant species worldwide.

Ethan Clayton, University of St Andrews.
Intramolecular covalent protein cross-links for protein engineering.
Dr Uli Schwarz-Linek, Prof. Gary Taylor, Dr Ian Wilkinson.

Intramolecular interactions in proteins have typically been limited to weak, non-covalent interactions, apart from disulfide bonds, previously thought to be the only prevalent covalent link within a protein. During the last decade, three new intramolecular, covalent cross-links within proteins have been found. The internal isopeptide, thioester, and ester bonds occur in abundance within Gram-positive bacterial surface proteins. All three of these cross-links form autocatalytically within the protein, with no external influence from enzymes or cofactors, and form in small, discrete domains. Thioester bonds appear to have a role in adhesion to the host, while isopeptide and ester bonds are likely structural domains, as they provide outstanding mechanical, thermal, and chemical stability to the proteins in which they occur. This project aims to exploit the unique properties of these cross-links for protein engineering applications. Primarily, we aim to utilise the exceptional stability afforded by isopeptide cross-links to stabilise proteins of pharmaceutical, and industrial interest, and explore expand upon current research and diagnostic applications of these cross-links. Success of this project could potentially lead to more stable pharmaceuticals, enabling better provision of leading medicines for third world countries, and could create improved biocatalysts to facilitate cheaper, greener, biofuel production.

1ST YEAR STUDENTS

Caitlin Connolly, University of Aberdeen.
How do Rif1 and SAF-A Remodel Chromatin Structure?
Anne Donaldson, Shin-ichiro Hiraga, Nick Gilbert.

To fit into the cell nucleus DNA is packaged into chromatin. Chromatin is crucial for regulation of DNA-related processes including replication, gene expression, and DNA damage repair. The Rif1 protein has been implicated in the organization of chromatin structure, but the underlying molecular mechanism is unclear. Recently our lab showed that Rif1 is a Protein Phosphatase 1-targeting subunit, meaning that Rif1 directs Protein Phosphatase 1 (PP1) to dephosphorylate specific substrates. This raises the possibility that Rif1 regulates chromatin by directing dephosphorylation of a chromatin component. In a proteomic screen for proteins showing increased phosphorylation upon Rif1 depletion, the chromosome scaffold protein SAF-A (Scaffold Attachment Factor A; also called HNRNPU) was identified. SAF-A can exist as a monomer or else form oligomeric chains, and SAF-A oligomerisation promotes chromatin decompaction. In contrast, prolonged SAF-A monomerisation promotes chromatin compaction and leads to the accumulation of DNA damage. I am testing the hypothesis that Rif1-PP1 dephosphorylates SAF-A to regulate chromatin organization and DNA damage repair. Specifically, I am testing the importance of two highly conserved PP1 recruitment motifs within the SAF-A sequence for chromatin compaction and domain organization. It is important to understand the relationship between chromatin structure and DNA repair so that new drug targets can be identified to treat diseases associated with DNA damage such as cancer.

Rory Craig, University of Edinburgh.
Developing Chlamydomonas reinhardtii as a study species for population genetics.
Prof. Peter Keightley, Prof. Nick Colegrave.

Despite the importance of Chlamydomonas reinhardtii as a model organism, the population genetics of the species remains largely unstudied. This partly stems from the difficulty of obtaining genomic data from natural isolates without extensive population structure, as well as the lack of a genome for any outgroup species. In light of this, we have generated population resequencing data for 24 C. reinhardtii natural isolates from a single population in Quebec, and we have been producing a de novo genome assembly for the most closely related known species, Chlamydomonas incerta, using the long-read sequencing platform ONT MinION. Utilising the high quality C. reinhardtii reference genome and these novel genomic resources, we will estimate nucleotide diversity and genetic divergence across various genomic regions and site class categories. We aim to further explore the nature of selective forces acting across these genomic site classes, with specific interest in characterising the extent of selective constraint in intronic and intergenic regions. In addressing such questions we hope to improve our understanding of fundamental evolutionary processes in both a general sense and specifically in Chlamydomonas reinhardtii. Alongside its use across various research fields such as plant genetics and physiology, this species is also used as a model for biofuel production, and it is hoped that our findings will positively impact these areas in the future.

1ST YEAR STUDENTS

Scott Dillon, University of Edinburgh.
No bones about it: unravelling skeletal biomineralization.
Professor Colin Farquharson and Dr Fabio Nudelman.

Many think of our bones as inanimate objects, but they are in fact extremely dynamic organs with very complex biology. Research has shown that our skeletons adapt throughout our lives to more effectively deal with the forces that we pass through them for example. These and the other functions of bone tissue are only possible given its complex and unique hierarchical structure. While many areas of bone biology remain mysterious, the question of its arrangement at the smallest ultrastructural level, and how this develops, remains particularly poorly understood.

Bone is made up of three major components – mineral which gives bone its strength and rigidity; collagen which gives bone a framework and a degree of elasticity; and other so-called non-collagenous proteins (NCPs). Several theories have been proposed as to how bone's ultrastructure is regulated. One of the most compelling is that the NCPs expressed by the cells during bone development perform essential functions in allowing mineral to infiltrate into and template upon the collagen fibril framework. Our project aims initially to analyse the gene and protein expression patterns of these NCPs in developing bone and correlate this with the ultrastructure. Ultimately we aim to elucidate how these proteins work in concert to regulate bone.

Many skeletal disorders are characterised by abnormal bone structure and mineralisation, such as hypophosphatasia, which represent significant debility. Our research could potentially lead new therapeutic targets for treatment of these diseases.

Juan Carlos Entizne, University of Dundee.
Construction and Refinement of Reference Transcript Dataset Annotations in plants.
John W. S. Brown and Runxuan Zhang.

Changes in gene expression are at the basis of the response of eukaryotic organisms to environmental or developmental signals. Regulation of the gene expression occurs at the transcriptional and post-transcriptional levels and include complex biological mechanisms such as alternative splicing (AS). Importantly, some genes are regulated only at the level of the alternative splicing generating AS isoforms without changing the level of expression of that gene.

RNA-seq provides information both at the gene expression and AS level. However, computational methods to analyse RNA-seq data accurately still need to be improved. RNA-seq data analyses are based on an initial reconstruction of putative transcripts from the sample and their subsequent quantification. However, studies have demonstrated that even the best performing transcript assembly methods present an accuracy inferior to the 50%.

Recent studies on Arabidopsis have shown that the quantification of transcripts, and subsequent analysis of differential expression analysis, are improved significantly by using a high-quality, comprehensive, non-redundant reference transcript dataset (RTD). The overall objective of this project is to develop a computational pipeline for the construction and refinement of high-quality RTDs and their use in gene expression analyses. The creation of high-quality RTDs will undoubtedly have big impact on bioscience research as it will allow researchers to perform faster and more accurate gene expression analysis on their studies.

1ST YEAR STUDENTS

Ivana Gachulincova, University of Edinburgh.
The Structural Basis of Pioneer Factors in Reprogramming to Pluripotency.
Dr Abdenour Soufi, Prof Ian Chambers.

About ten years ago, Shinya Yamanaka has taken the scientific community by storm as he and his team have converted mature cells to immature stem cells called induced pluripotent stem cells (iPSCs) that have a unique potential to become any cell type of our body. This basically means that one can make any cell type like neurons, liver, and heart cells, from the patients themselves, which can then be used to repair the damaged tissue or organ or model a disease to make patient-specific drugs. The other advantage of this reprogramming technology is its simplicity as iPSCs can be generated from adult skin cells by adding only four genes. However, reprogramming of human cells to iPSCs is still a very time-consuming, unreliable, and inefficient process. The four reprogramming genes are also known for their association with cancer, making this method risky to use in patients. To overcome these limitations, we need to first understand how reprogramming works. This study focuses on one of the four genes called Oct4, and aims to reveal the three-dimensional structure of Oct4 in complex with its target nucleosomes. Nucleosomes are the core packaging units of the genome, which is uniquely packaged in each cell type. So, understanding this molecular interaction at the atomic level will help us uncover how to control cell identity. Ultimately, this will help to improve the efficiency and fidelity of reprogramming to any cell type. Improvements in reprogramming technology will be highly beneficial for biomedical research and clinical medicine.

Grant Gale, University of Edinburgh.
Engineering Solar Powered Cell Factories for Sustainable High-Value Chemical Production.
Dr Baojun Wang and Dr Alistair McCormick.

Cyanobacteria are ancient solar powered cell factories with the ability to make all of their own complex organic molecules from only carbon dioxide, water and a few trace minerals all powered by the energy of the sun. Cyanobacteria, which are also known as blue-green algae, utilise a suite of special light harvesting pigments called phycobiliproteins as well as chlorophyll, to enable them to convert the sun's energy into chemicals through a process called photosynthesis. Phycocyanin-C is one particular naturally occurring light harvesting pigment-protein complex, has a rich blue colour and which gives the cell access to a greater range of the light spectrum than it would otherwise have. Phycocyanin-C has some useful properties including being a potent antioxidant, use as a natural food dye and colourant and also very special fluorescence properties which are valuable to the pharmaceutical industry. Cyanobacteria produce Phycocyanin-C naturally but in industrially relevant production scales, they can be difficult to grow reliably. The reason for the unreliable production is it is difficult to ensure that all of the cells get the required amount of light to enable them to photosynthesize. This project is investigating the possibility of genetically engineering new capabilities into cyanobacteria to enable them to grow under a wider set of conditions. This is a proof of concept project and if successful, the aim will be to further engineer these organisms to produce biofuels, biomaterials and vaccines, all with just light energy which can be powered from renewables helping to achieve a sustainable future.

1ST YEAR STUDENTS

Michael Gallagher, University of Aberdeen.
Novel genomics-led approaches to characterise viral diseases in Atlantic salmon.
Dr Daniel Macqueen; Dr Iveta Matejusova.

Global production of salmonid fishes in aquaculture is worth > £8 billion annually, accounting for ~15% of total traded farmed fish. However, a major bottleneck to expansion in the industry is losses caused by infectious diseases, which can have devastating economic impacts. Viruses - which cause 20% of all known infectious diseases in aquaculture - are of particular concern as a distinct lack of effective anti-viral therapeutics or preventative vaccines have been developed. For example, an outbreak of Infectious Salmon Anaemia virus (ISAV) in 2007-08 cost the Chilean salmon industry around $1 billion and reduced the salmon production from 650,000 tonnes to just over 100,000 tonnes in just two years. Rapidly and accurately diagnosing viral outbreaks can help control strategies by identifying the strains and subtypes present and their associated pathogenicity. The current industry standard is to sequence single viral marker genes. My project is developing approaches to routinely and affordably sequence whole genome sequences for problematic salmonid viruses using second (Illumina) and third generation (Oxford Nanopore) sequencing platforms. The goal is to enable robust and rapid genome-wide analysis and diagnostics, and to facilitate improved implementation of molecular epidemiology for inferring transmission routes and linking sequence variation to pathogenicity. Applying such technologies to the aquaculture industry may ultimately help control the spread of devastating diseases and contribute to both economic and food security.

Imogen Johnston-Menzies, University of Edinburgh.
Investigating differential virulence of Salmonella serovars in livestock animals.
Jo Stevens; Andrew Gill.

Salmonella enterica is a major bacterial pathogen of global importance for both human and veterinary medicine. Farmed animals, as a source of food and environmental contamination, represent a critical reservoir for human food poisoning, where over 85% of cases of salmonellosis are considered food-borne. In 2008 alone, Salmonella infections in humans cost the European Union over £14 million, a tentative figure that excludes the agricultural impact of Salmonella.

S. enterica serovars of greatest veterinary threat to animal health and food security in the UK are Typhimurium, Choleraesuis, Dublin, and Gallinarum. These serovars differ most fascinatingly by host adaptation. This differential virulence showcased in different animal hosts by each of the serovars is a well-documented area of veterinary medicine, but the underlying molecular mechanisms controlling host range have yet to be fully understood.
The type III secretion system, critical for Salmonella pathogenesis, is a molecular syringe that injects over 30 proteins into host cells where they manipulate the host immune response and cellular function. We predict that differences in the repertoire of these secreted proteins between the serovars controls host range. This study aims to use proteomics and mass spectrometry, a technique that measures the molecular weight of digested proteins, to identify and quantify the proteins secreted by each serovar to determine whether differences in protein repertoire or in the amount of protein secreted, underlies host adaptation.

This greater understanding of host adaptation would not only inform future vaccination strategies in livestock but also reduce the global economic impact of salmonellosis.

1ST YEAR STUDENTS

Clare Latta, University of Edinburgh.
Understanding inflammation in the brain during ageing.
Barry McColl and Rona Barron.

The brain has several approaches to fight against an injury or infection. A key approach requires specific cells in the brain, termed microglia. These cells can identify objects that do not belong there and cause damage such as bacteria, viruses or fragments released from dead cells. Microglia defend the brain matter by consuming and releasing substances to break down these objects and therefore lessen the harm to a person. However, as we age, microglia become less able to react appropriately to remove these harmful objects and repair damaged cells.

A protein found on the surface of microglia termed TREM2, triggering receptor on myeloid-2 cells, plays an important role in guiding the response of microglia to harmful objects. Studies on the genetic information of a large sample of people have shown that abnormal changes in the genetic code for TREM2 increases the risk of several age-related diseases of the brain including Nasu-Hakola disease, Alzheimer's disease (AD), Parkinson's disease (PD) and Amyotrophic Lateral Sclerosis (ALS). Therefore, TREM2 is predicted to have an important role in maintaining a healthy brain. The aim of this project is to understand the function of TREM2 and its role in age-related brain diseases.

Overall, this project will explore a major factor that increases the risk of brain diseases with increasingly high incidence in society. In the big picture, it will contribute to understanding a potential target for treatment, improve public health and will minimise the substantial burden of age-related brain diseases on the economy.

Kerry Leslie, University of St Andrews.
Core effectors of plant-parasitic nematodes and their host targets.
Sebastian Eves-van den Akker, Sophie Mantelin, John Jones.

Plant parasitic nematodes (PPN) parasitise many major food crops such as potatoes, tomatoes and soybean. PPN cause damage valued at approximately 80 billion U.S. dollars in crop loss per year. Many nematode species must form a feeding site called a syncytium in the roots of their host plant to survive. However, there is still relatively little known about how PPN initiate and maintain their syncytia. In order to successfully parasitise their host, PPN, like other plant pathogens, have evolved specialised proteins known as effectors: pathogen proteins and small molecules that alter host-cell structure and function.

The aim of this project is to identify a core set of effectors present and expressed in four syncytia-forming nematode species; Globodera rostochiensis, Globodera pallida, Rotylenchulus reniformis and Nacobbus aberrans. Characterisation of a basal set of effectors that these nematodes utilise in syncytia formation will allow greater understanding of syncytium maintenance and suppression/ avoidance of host species immune responses. Comparisons between the effectors present in these species suggest that 37 gene families are conserved across these nematodes. A subset of these core effectors will be functionally characterised and their subcellular locations identified. Current work is focused on a novel cell wall degrading enzyme that is present in three of the four species.

1ST YEAR STUDENTS

James MacLeod, University of St Andrews.
Optogenetic dissection of Locomotor Networks in Drosophila melanogaster larvae.
Dr Stefan R Pulver and Dr Wenchang Li.

Animals, including humans, don't use their brains to produce repeating patterns of movement such as walking, chewing, breathing or swimming. Instead, the rhythms required for these movements are produced in the spinal cord and are activated or modified by the brain. These simple pattern producing modules are called "central pattern generators" or CPGs. I study these neural networks in the larvae of fruit flies by recording their activity and activating or deactivating groups of nerve cells in these networks using light.

Understanding how these simple networks function helps us understand the principles of how nervous systems are built and how they are organised. For example, one of the key things the brain does is produce waves of activity known as 'brain waves', studying how wavelike activity is produced and propagated in fruit fly larvae can help us understand how they're made in the far more complex human brain.

We also hope to use our chosen system to understand how groups of neurons work together to make decisions. The fruit fly ventral nerve cord (their equivalent to a spinal cord) spontaneously changes between different forms of locomotion, the decision to change locomotor state can be influenced by light manipulations, drugs, genetics and behavioural experiments. This gives us a great opportunity to investigate what information this simple neural network is using to make its decisions and what physical form these decision making networks actually have.

Kate Mathers, University of Dundee.
Harnessing bacterial weaponry in the fight against antibiotic resistance
Dr Sarah Coulthurst

Antibiotic resistance is currently one of the biggest threats to global health. Without new antibiotics, it is estimated that ten million people will die each year from antibiotic-resistant infections by 2050, overtaking cancer as the world's single biggest killer. There has never been a more pressing need to develop new types of antibiotics in the fight against bacterial infections. So why not use the antibacterial strategies of bacteria that have evolved specifically to destroy other bacteria? This approach showed promising results last year when an antibacterial protein produced by the bacterial species Staphylococcus lugdunensis was found to act as an effective antibiotic in animal models.

Another antibacterial strategy used by bacteria is the Type VI Secretion System (T6SS), a microscopic weapon that bacteria use to inject antibacterial proteins (effectors) directly into other bacterial cells. The T6SS contains a spiked spear-like structure that is propelled from the surface of the bacterial cell and carries the antibacterial effectors into neighbouring cells, thereby killing any competitors. The aim of this project is to investigate the antibacterial T6SS effectors of two bacterial species: Serratia marcescens and Klebsiella pneumoniae. Although S. marcescens is known to produce antibacterial T6SS effectors, the T6SS has not yet been studied in K. pneumoniae. By studying the T6SS effectors of these species, we may be able to harness their antibacterial power to develop a new class of antibiotics, essential for the global fight against antibiotic resistance.

1ST YEAR STUDENTS

Isobel McLachlan, University of Edinburgh.
Dynamic Modelling of Foot and Mouth Disease in Endemic Areas.
Mark Bronsvoort, Ian Handel, Glenn Marion, Ian McKendrick.

Foot and mouth disease (FMD) virus, affects cloven-hooved animals including cattle. It is economically costly due to direct impacts on growth rates and milk production and through impact on international trade and movement of animals or their products. Globally it is the most important disease of livestock. Introduction of FMD to disease free regions, including Europe and North America, is a major concern. Continuing circulation of FMD virus in many parts of Asia, Africa and the Middle East is somewhat overlooked and poorly understood including the role of persistently infected “carriers” which is difficult to study in the field.

Computer-based simulation of disease spread can be used to further understanding of FMD dynamics. Current simulations mostly investigate outbreaks in largely susceptible temperate farming systems. In contrast, endemic systems in the tropics and subtropics typically have greater herd mobility, more frequent contact between herds, poorly controlled open boundaries and pre-existing immunity. These differences make most existing models unsuitable for understanding disease dynamics in farming systems characteristic of FMD endemic areas.

This project utilises dynamic mathematical modelling to further understanding of FMD epidemiology in endemic regions like Cameroon in Central Africa. Suitable models should address important aspects of endemic disease systems and capture patterns of disease observed across different regions and seasons. These can then be used to explore key epidemiological questions regarding the role of “carriers”, the geographical and population scales at which disease persists as well as the impacts and thresholds for control strategies such as vaccination and movement controls.

Zandile Nare, University of Edinburgh.
RNA Editing Ligase 1 (REL1) as a therapeutic target for trypanosomatid diseases
Achim Schnaufer.

Trypanosomatid parasites are responsible for causing a variety of neglected tropical diseases that kill more than 100,000 people annually and put millions of people at risk. Trypanosoma brucei (Tb)causes African sleeping sickness in humans and nagana in horses and cattle. The combined effects of the human and animal trypanosomiases have a profoundly negative impact on agricultural development and productivity thereby stifling the socioeconomic development of affected communities. Current treatments for trypanosomatid diseases are inadequate thereby necessitating the development of novel anti-trypanosomatid therapies. A unique feature of kinetoplastid parasites is their ability to utilise RNA editing for mitochondrial gene expression. Key enzymes in this process are REL1, REL2 and KREPA2. REL1 is an attractive drug target for African sleeping sickness because; (1) REL1 is essential for the survival of the parasite, (2) there is no mammalian homologue and (3) a 1.2 Å crystal structure of the catalytic domain of TbREL1 is already available. High throughput screens (HTS) of several compound libraries have identified a number of ‘hits’ against TbREL1. My research aims to; (1) develop and optimise a surface plasmon resonance based assay for the validation of primary hits againstTbREL1, (2) develop and optimise expression and purification protocols for different trypanosomatid REL2 orthologues, (3) structural and functional analysis of TbREL1-KREPA2 and REL2 orthologues, (4) establish REL2 as a model system to complement REL1 drug discovery and (5) utilise virtual HTS platforms (i.e. LIDAUES & AutoDock Vina) to identify additional lead compounds and/or lead scaffolds for REL1 drug discovery.

1ST YEAR STUDENTS

Jessica Powell, University of Edinburgh.
Using Epigenetics to Characterise the Cattle Immune Response.
Liam Morrison, James Prendergast and Tim Connelley.

Infectious diseases of cattle are one of the biggest constraints on agriculture in low and middle-income countries (LMIC), for example, African Animal Trypanosomiasis alone is estimated to cost over US$ 4.5 billion per annum. However, African cattle breeds remain considerably less well studied than commercial European breeds in this context. While research into improving disease resistance in cattle has focused on genetic components, there is increasing awareness of the importance of epigenetics. Epigenetics is the study of changes in gene expression, for example when genes are switched on or off, without modification to the underlying DNA sequence. However, the tools to enable the study of cattle epigenetics are almost entirely lacking.

In this project epigenetic profiles of major blood cell types involved in the immune response will be created for European and African taurine (Bos taurus taurus) cattle and African indicine (Bos taurus indicus) cattle. The project aims to use the unique profiles generated to statistically estimate the proportion of each cell type in whole blood. This method could be easier and more informative than current laboratory methods. Subsequently, changes in the composition of different cell types in blood following infection can be investigated. Diversity in the epigenome of African and European cattle subspecies will be analysed to identify regions of DNA linked to expression of advantageous traits, such as disease resistance. The exploitation of such heritable traits provides the potential to improve cattle productivity in LMICs and reduce the economic impact of infectious diseases.

Charlotte Repton, University of Edinburgh.
The role of Microtubule-Associated Proteins in meiotic spindle formation.
Professor Hiro Ohkura, Dr Heidrun Interthal.

My research concerns the segregation of chromosomes in female meiosis. Errors in this process are the leading cause of birth defects (such as Down Syndrome), infertility and miscarriage in the UK. Unlike in mitosis, female gametes eliminate their centrosomes before dividing. The impact of this is not fully understood. My project looks specifically at the proteins associated with the microtubule spindle in the dividing oocyte. We plan to identify the entire set of microtubule-associated proteins (MAPs) and investigate the roles of a subset of these. Currently, the only predictor for aneuploid pregnancies is mother's age. A potential outcome from my research would be better screening for risk of Down Syndrome and other genetic syndromes arising from chromosome mis-segregation.

1ST YEAR STUDENTS

Deon Roos, University of Aberdeen.
A multiscale bio-economic approach to optimising rodent crop pest.
Prof. Xavier Lambin, Dr Bea Arroyo, Dr Francois Mougeot and Prof. Juan Jose Luque-Larena.

Rodent crop pests cause substantial damage to agriculture every year. In Indonesia alone, rodent crop pests consume the equivalence in food that could feed 60% of the Indonesian population. My PhD is focused on developing the ecological understanding of a specific crop pest, the common vole (Microtus arvalis), and how to include this information in the management of this species. Crucially, however, the intention behind the research is to provide a framework for how other similar rodent crop pests may be controlled in other parts of the world.

Through investigating the relationship between pest density and the associated damage caused to crop yields; exploring any potential negative impacts of control strategies as well as their overall effectiveness; using large scale spatial movements of the cycling population to identify potential weakpoints, or bottlenecks; will allow this and other information to be incorporated into an adapative management plan, one that will hopefully provide an evolving approach to the problema, that improves with increasing understanding and experience. Crucial to this aim will be the inclusion of local stakeholders, farmers, conservationists, government bodies and members of the public to ensure that any outcome is one that can realistically be adopted into the farming society. Consequently, the use of game theory and similar social science methods is intended to demonstrate the value of a combined and collaborative effort in tackling the problem in a way that is amicable to all stakeholders.

Jenn Ross, University of Edinburgh.
The Structure and Function of Encapsulated Ferritins
Dr David Clarke and Dr Jon Marles-Wright.

Iron is essential to life but needs to be managed carefully within cells as it can react with oxygen and make toxic products that can damage DNA and proteins in the cell.

Ferritins are proteins that form spherical cages that can safely store iron by turning it into an insoluble mineral, which cannot react further. A new type of ferritin, called encapsulated ferritin (EncFtn) does not form its own cage, but instead uses a separate protein cage, encapsulin, as an iron storage system.

To understand how these proteins work to store iron, I will use various techniques to image and investigate their structure and function. I will establish the stability, size, iron-binding capacity of the encapsulin system. Once these facts are known, I will be modify the system to hold other metals and maximise its storage capacity.

Ultimately, this system will have applications in medicine and environmental science. The encapsulin cages can be used to hold medicine to be distributed around the body. This has been achieved with the cancer drug, cisplatin, which was held inside a ferritin protein cage and delivered to a tumour where it dismantled to release the drug. Encapsulated ferritins are much larger than typical ferritins, so have the potential to store more of the drug or larger drug molecules. A ferritin is currently used in a water treatment to reclaim phosphate, as phosphates are stored with iron in the ferritin cage. The large size of encapsulated ferritins potentially allows greater storage of iron and phosphates, which could lead to an improved water purification treatment.

1ST YEAR STUDENTS

Eevi Savola, University of Edinburgh.
Dietary restriction and stress: Exploring Drosophila life-history trade-offs and ageing.
Dr. Craig Walling and Dr. Pedro Vale.

Currently parts of the world are observing a constantly growing ageing population. Therefore, we need to understand different variables affecting lifespan and ageing. One such potential variable is diet. Dietary restriction (DR), limiting a certain nutrient or overall caloric content of food, is often considered to extend lifespan whilst limiting reproduction. Recent studies have suggested genetic and environmental variation in the response to DR. Stressful environments have shifted the optimal macronutrient compositions for some organisms. A new theory to account for this variation, and to explain the lifespan extension under experimental conditions, is that DR is a laboratory artefact. In more stressful conditions, DR will not extend lifespan. We used a genetically diverse population of fruit flies (Drosophila melanogaster) reared on 10 diets in a range of protein to carbohydrate ratios. In Drosophila, DR seems to be facilitated through protein and not calorie restriction. With a pinprick underneath the wing, a subset was injured with a clean pin or infected by a pin dipped in a bacterial solution. Throughout the flies' lifespan, the total numbers of eggs laid, climbing ability and gut robustness were measured. Aging was measured as the decline in these traits over time. The results of this experiment allow testing of this theory and to understand the role of macronutrient balance in different environments. This may further understanding in how diet influences health and ageing, or which diet compositions may be more beneficial in different circumstances.

Guillermo Serrano Nájera, University of Dundee.
Cell and tissue dynamics driving gastrulation.
Kees Weijer, Silke Henkes, Rastko Sknepnek.

Animal bodies are shaped throughout embryonic development. During this process, the cells of the developing embryo divide, move, change their shapes and die in an organized way to produce all tissues and organs. However, how these cell behaviours are coordinated both, in time and space, through thousands or millions of cells is currently unknown.

To answer this question, we study gastrulation in chick embryos. Before this stage the chick embryo is a circular layer of around 20000 cells floating on top of the yolk. During gastrulation a group of cells located in the periphery move to the mid-line forming a groove, known as the primitive streak. Once the cells reach the streak they ingress inside the embryo to form the three embryonic layers. Furthermore, this remarkable structure is going to define the longitudinal and transversal axis of the animal. Understanding the mechanisms of coordination underlying the massive reorganizations during gastrulation is the main aim of this investigation.

To study chick gastrulation, a light-sheet microscope was fabricated. This novel tool is able to image with cellular resolution whole fluorescently labelled embryos in vivo. Using computational routines we can analyse the images and assess the behaviours of the individual cells. This approach, in combination with chemical and mechanical perturbations of the embryo, will allow us to understand how cells are organised during gastrulation. Finally, to test our hypothesis, we will create full-scale computational models of gastrulation based in soft and active matter physics in collaboration with two theoretical groups.

1ST YEAR STUDENTS

Jennifer Shoesmith, University of Dundee.
The Characterisation of Three Genes Involved in Barley Architecture.
Supervisors: Dr Sarah McKim, Dr Kelly Houston.

Barley is the fourth most cultivated cereal crops in the world. As well as being used in malting, a significant amount is used as animal feed as well as for human consumption. During the green revolution the introduction of semi-dwarf varieties of crops resulted in an increase in yield because shorter plants are less susceptible to lodging. Therefore, changes in plant architecture can lead to higher yielding plants. In this project we are investigating the function of three genes, which are regulators of gene expression. Due to their similarity these three genes are part of a gene family. In other cereal crops such as maize and rice these genes have been shown to contribute to variation in architectural traits such as plant height and branching. We aim to investigate how these genes influence architecture in Barley plants. We aim to do this by switching off these genes and over expressing the gene in Barley, and see how this mis-regulation affects architecture. This information could then be used to make higher yielding barley cultivars either by directing breeding programmes or through the generation of transgenic plants

Andrew Strange, University of Aberdeen.
Finding the pieces of the puzzle: autism and protein synthesis.
Dr Berndt Müller, Dr Christos Gkogkas and Professor Colin McCaig.

Autism spectrum disorder is an umbrella term covering a range of mental disabilities, which affect 1 in around 100 of us. Autism spectrum disorder is characterised by repetitive behaviours such as completing the same task at the same time every day, as well as problems with social contact, such as avoiding eye contact or being unable to pick up on non-verbal cues. Autism spectrum disorder includes high functioning autism, Asperger syndrome, and ADHD among other conditions. We and others have found earlier that one specific protein called eIF4E, whose normal function is to control protein synthesis, predisposes to the development of autism when too much of it is present in the brain. My work focuses on understanding how increasing the amount of eIF4E causes the development of autism spectrum disorder. I am investigating the effect of increasing eIF4E on the control of protein synthesis and network formation in cultures of neuronal cells, as it is under normal circumstances not possible to study neurons obtained directly from living people with autism spectrum disorder. By doing this I am able to study at the level of cells how brains of autist individuals may work, and to compare this to neurons representing neurotypical brains. The outcome of my work is a better understanding of the causes of autism and how it develops. Hopefully, this will contribute to being able to develop cures and treatments for autism spectrum disorders.

1ST YEAR STUDENTS

Marcos Valenzuela-Ortega, University of Edinburgh.
Development of novel methods for high throughput screening of recombinant constructs for conversion of cellulosic biomass to useful products..
Prof. Chris French, Alistair Elfick.

There is an increasing need to leave fossil fuels behind as source of energy, combustion fuels and chemical industry feedstock, due to the environmental impact and increasing scarcity. Recent advances in biotechnology exemplify the production of several types of biofuels and a wide range of interesting chemicals obtained from greener renewal resources, thus potentially replacing fossil fuels.

Glucose is the main building block of metabolism, commonsubstrate to many of the processes to produce biofuels and biochemicals. Nonetheless, glucose is currently obtained from food crops and its biotechnological use can rise food prices. Lignocellulosic biomass is an interesting alternative. Plant lignocellulose is mostly cellulose, a glucose polymer. However, due to its molecular structure, depolymerisation of cellulose to a profitable glucose requires of the coordinated activity of several enzymes, and this capacity is limited to very few organisms in nature. Because of this, this interesting prime material is hard to introduce to biotechnological processes.

Recent publications have shown production of biofuels from cellulosic biomass, but the results are far from being cost-effective. This project aims to improve the yield by finding enzymes that can be secreted by a fermenting microorganism, which will transform cellulose in a useful product. New methodologies will be generated to allow high-throughput generation of genetic variants and high-throughput selection of these. The screening methods will be based on integration of diverse technologies based on DNA assembly methodologies, robotics, microfluidics, and new genetic selection systems such as biosensors.

Jennifer Wardle, University of Aberdeen.
Resolving the Conflicting Demands on Organic Wastes in Rural Ethiopia.
Jo Smith, Anke Fischer, Lisa Avery, David Vega-Maza.

Population growth and associated localised deforestation in rural Ethiopia is having an impact upon soil quality and hence food security. Up to 99% of the rural community is dependent on biomass as fuel for cooking. As the number of nearby trees declines, more crop residues and dried cow dung are used as a replacement fuel on inefficient 3-stone fires. These materials were previously returned to soils, replacing a proportion of the carbon and nutrients harvested. This decrease in replenishment has a derogatory impact upon the already low-carbon, drought-prone soils.

Increasing the flow of organic matter back to the soils would improve the soil structure, increase its water-holding capacity and reduce the demand for expensive inorganic fertilisers. Combining improved cooking stoves with anaerobic digestion and composting of existing and new inputs could offer an environmentally and financially sustainable solution. Anaerobic digestion can provide a source of clean-energy fuel and homogenise the organic matter into a pathogen-reduced, high-nutrient fertiliser. In water scarce conditions the organic materials can be composted. This retains a higher carbon content than anaerobic digestion but cannot supply energy. New designs are in progress that allow anaerobic digestion in water scarce environments.

Transitioning from biomass to biogas burning has multiple advantages out-with the environmental benefits. Human health is improved by the reduction of smoky indoor fires and reduced exposure to untreated faecal matter in water supplies. In addition to this, empowerment is gained from the time saved from fire-wood collection, allowing further social or economic activity..

1ST YEAR STUDENTS

Luke Woodford, University of St Andrews.
Improving honey bee colony health – coordinated control of Varroa destructor.
Prof David Evans, Dr Alan Bowman.

Honey bees are key pollinators of agricultural crops and other important plant species. Honey bee colony losses have a large impact ecologically and economically. Globally, honey bee colonies are infested with a mite, Varroa destructor, which transmits a range of viruses. The most important virus is deformed wing virus (DWV). ~25% of colonies are lost annually, the majority due to Varroa-transmitted infections. Effective miticide treatments are available and improve colony health. However, there is no real attempt at rational treatment regimens to maximise their efficacy. This study will use coordinated treatment of Varroa in a geographically isolated environment (the Isle of Arran). The aim is to show that rational, coordinated treatment improves colony health. “Healthy” and “unhealthy” virus population profiles have been determined in earlier studies. A high level of a near-clonal virus population indicates poor colony health, whilst low levels of a diverse population of DWV strains is typical of healthy colonies with low/no Varroa levels. We will sample bees from colonies before and after miticide treatments and measure changes in the virus levels and diversity in the population. By doing so we will be able to determine if the treatment regime is improving colony health – reducing virus levels and increasing diversity - across the whole island. The geographic isolation will reduce the impact of bees moving into the area. This pilot study will determine whether coordinated treatment is beneficial at the landscape scale, and will form the basis of larger trials if successful.

Charlotte Woolley, University of Edinburgh.
Investigation into the causes of vomiting and diarrhoea in dogs.
Clements, Dylan. N., Handel, Ian. G., Broonsvoort, B. Mark., Schoenebeck, Jeffrey. J.

Stomach upsets in dogs such as vomiting and diarrhea are common, unpleasant for dog owners and are not well understood. Sometimes, they can be financially expensive and lead to more serious health problems. The main aim of this project is to find out what makes stomach upsets more likely in some dogs compared to others. For example, could it be due to their lifestyle, genes or where they live?

We will use information from Dogslife to find out more, which is a research project that collects a variety of information about thousands of Labrador Retrievers in the UK. Owners involved in the project complete regular on-line questionnaires throughout their dogs lives. However, we need to remove any obvious errors (e.g. typos) before we can use this information. This is known as “data cleaning” and helps to make sure that information is high quality. We have developed an automated data cleaning process for the age, sex, colour, height, weight, health and lifestyles of dogs. The method uses a combination of investigation, mathematics and rules to allow us to quickly remove errors from the information provided.

In the future, we also plan to collect information about the organisms that live inside dogs’ guts and about the type of Google searches people use to find out about dogs’ stomach upsets. We hope that this project will improve our understanding of stomach upsets in dogs and potentially help vets and dog owners to make it less likely that their pets will develop these problems.

1ST YEAR STUDENTS

Joshua Wort, University of St Andrews.
Investigating a Novel Copper-based Label for Pulsed EPR Applications.
Dr Bela E. Bode, Dr David G. Norman.

In recent years structural biology has started to focus on large, multi-subunit systems, that are relevant in the development or delay of disease. This is because the structure of bio-macromolecules is intimately connected to their function; and a holistic approach is optimum for understanding both the mechanism and pharmacokinetic profile of therapeutic agents such as antibiotics and anti-cancer medications, operative on such systems. Problematically, a number of work-horse techniques: x-ray crystallography, cryo-EM and NMR have encountered obstacles when studying large, complex or dynamic structures for one reason or another. Pulsed EPR spectroscopy is another technique that is an indispensable tool in this regard, interrogating systems in a longer distance range. In brief, pairs of labels, each containing an unpaired electron, are introduced to the system under investigation and the inter-spin distance is determined. Further mathematical treatment generates a distribution of these distances, related to the conformational space sampled by the system, in real time. Thus, while the technique can be applied to larger systems of interest, it is often limited by poor resolution at long distances, related to the flexibility of the label within the molecule. Our research attempts to better characterise a particular label, to provide extremely high resolution structural information in large systems. By combining previous findings that allow measurement of significantly longer inter-spin distances, and high label rigidity; we hope to show that even for longer distances, resolution is conserved.

Alina Zitskaja, University of Aberdeen.
The Impact of Phytochemicals on Adipose Tissue Function and Obesity.
Dr Andreas Kolb, Dr Justin Rochford.

Obesity is a metabolic disorder resulting from an imbalance of energy intake and expenditure, such that health is adversely affected. Recent advances in thermogenic adipocyte biology point at alternative approaches to treating obesity. Brown adipose tissue (BAT), a major energy dissipating organ, metabolises fat and glucose into heat through thermogenic respiration in the mitochondria. BAT-mediated energy expenditure is driven by the mitochondrial uncoupler protein 1 (UCP1), and has been shown to protect against obesity and diabetes. Activating BAT, and promoting BAT-like features in the fat-storing white adipose tissue (WAT) are therefore attractive therapeutic approaches to treating obesity.

Phytochemicals in blueberry extracts have been shown to prevent obesity in C57B/6 mice fed a high fat diet. The mechanisms underlying the beneficial effects of phytochemicals on metabolic health are currently unclear, and require further research to allow their effective application.

This study investigated the capacity of blueberry extract (BBE) to act as an anti-obesity agent. The 3T3-L1 cell line was used as an adipocyte model to elucidate BBE ability to increase energy expenditure by thermogenesis. Gene expression signatures unique to ‘browning’ of adipocytes were analysed by qPCR. Subsequently, mitochondrial biogenesis was assessed by qPCR and live cell imaging. BBE was shown to upregulate UCP1 gene expression and increase mitochondrial biogenesis in mature 3T3-L1 adipocytes. Taken together, these findings suggest that dietary BBE may represent a promising target for diet-induced remedy of energy imbalance, and could form part of obesity prevention strategies.

2ND YEAR STUDENTS

Eloise Ballard, University of Aberdeen.
Antifungal resistance: a global problem.
Prof Adilia Warris, Prof Al Brown, Prof Paul Verweij

Fungal infections kill 1.5 million people around the globe each year. These infections mainly affect individuals with compromised immune systems and are caused by a variety of fungi. This project focuses on the fungus Aspergillus fumigatus which mostly causes lung infections. Aspergillus infections are obtained via inhalation of tiny spores into the lungs. The most common drugs used to treat these infections are azole antifungals. Unfortunately, these antifungals are becoming increasingly ineffective due to the development of antifungal resistance.

Azole resistance can develop both in a hospital environment, within the patient, or in our community. Azoles used in various non-hospital locations are comparable to those used clinically to treat human infections. For example, azoles are used in wallpaper paste to prevent mould growth on walls, and in agriculture to protect crops from fungal disease. Exposing Aspergillus to azoles in any environment has the potential to cause drug resistance. As a result, patients are at risk of becoming infected with Aspergillus strains resistant to azoles. This makes the treatment of these infections really challenging.

This project investigates the mechanisms by which Aspergillus can become resistant to azoles in a hospital environment. This research will improve our understanding of how Aspergillus becomes resistant to azoles and will consequently give new leads to improve treatment regimens with a direct patient benefit.

Svetlozara Chobanova, University of Aberdeen
Generating an Orthogonal Translation Compartment in Yeast
Dr Jonathan Pettitt, Dr Berndt Müller and Prof Ian Stansfield

Spliced leader (SL) trans-splicing occurs in many eukaryotes including nematodes such as Caenorhabditis elegans and Ascaris suum. It represents the transfer of a short SL RNA sequence to the 5’ end of messenger RNAs (mRNAs). The SL RNA is trimethylguanosine capped, and this cap is thus donated together with the SL to the mRNA via the trans-splicing mechanism. This event provides the necessary 5’ end cap structure for mRNA stabilisation and translation. We are interested in exploiting this process to generate an orthogonal translation system in Saccharomyces cerevisiae and thereby improve the synthesis of exogenous protein expression. Our preliminary experiments show that expression of SL RNA is sufficient to confer this activity in S. cerevisiae cells. By expressing orthogonal translation initiation factors coupled with the expression of specific messenger RNAs, translation initiation in S. cerevisiae can be controlled, so it is directed to a messenger RNAs of interest. Improved translation of mRNA of interest, due to an orthogonal translation compartment could lead to increased specificity of protein production, where the synthesis of a protein of interest is improved and easily controlled. A controlled protein production could be a powerful technological platform for satisfying the demand of efficient protein synthesis on industrial scale.

2ND YEAR STUDENTS

Morag Clinton, University of St Andrews.
Alterations in Salmonidae gill tissue in response to harmful environmental organisms.
Dr David Ferrier, Prof Andrew Brierley, Prof Sam Martin.

The focus of this project is to investigate the impact of harmful phytoplankton and zooplankton present in the environment on farmed fish, specifically Atlantic Salmon and Rainbow Trout. Like all farmed animals, fish can suffer from a number of diseases,although the full impact of many on the health of fish is still not known. Both phytoplankton and gelatinous zooplankton, more commonly known as jellyfish, are known to cause damage to delicate fish gill tissue, however the mechanisms for this damage are still poorly understood. Damage to gills impacts the health of the animals and profitability of their production.

This project investigates how the immune system responds to this damage, as well as how the normal healthy bacteria present on the gills can alter after exposure to these harmful organisms. Improved knowledge of what changes occur from exposure of fish to these harmful organisms can inform how best to mitigate their effect, and help improve how we care for farmed fish. Aquaculture is a large and expanding industry in Scotland, but it can only continue to increase production if the welfare of fish is safeguarded.

Sophie Donovan, University of Edinburgh.
Re-engineering photosynthesis: editing RuBisCO in higher plants with CRISPR/Cas9.
Alistair McCormick.

The enzyme RuBisCO (ribulose-1,5-bisphosphate carboxylase/oxygenase) catalyses net CO2 assimilation in all photosynthetic organisms. However, RuBisCO is slow and cannot fully discriminate between O2 and CO2. Improving the performance of RuBisCO could significantly increase the productivity of C3 crops, such as rice and wheat. The RuBisCO complex is comprised of a chloroplast-encoded large subunit carrying the catalytic site and nuclear-encoded small subunits (SSUs), which may play an important role in determining the catalytic rates. Understanding the significance of SSU variation on RuBisCO's catalytic efficiency in planta is challenging due to lack of a suitable species for SSU transformation. In higher plants, SSUs are encoded by large rbcS gene families composed of 4-22 isoforms, which has hindered the generation of multiple SSU knockout mutants. This study is using the CRISPR/Cas9 system to knockout the native rbcS family from the model species Nicotiana tabacum (tobacco). We aim to develop a tobacco genotype that can be used as a platform where non-native SSUs can be tested to explore their contributions to the catalytic properties of RuBisCO. Understanding the role of the SSUs on RuBisCO catalysis will potentially influence strategies that aim to improve photosynthesis for increased crop yields.

2ND YEAR STUDENTS

Sophie Edwards, University of St Andrews.
Physical cognition and nest building in birds.
Susan Healy, Simon Meddle.

Emily Fowler, The University of Edinburgh.
Role of the dPIAS in heterochromatin formation.
Patrick Heun.

All of the DNA in a cell needs to be packaged into a small space. The DNA is organized for it to be properly read, leading to packaging known as chromatin. There are two district types of chromatin: heterochromatin- which is tightly packaged and therefore to a great extent is not used by the cell and euchromatin- which is more open and therefore readable. Upon chromatin is a layer of instructions for its use, known as post-translational modifications, which are important for determining heterochromatin versus euchromatin and thus determining the balance between gene repression and gene expression. In different cells or at different times both the chromatin and the post-translational modifications are different and this is responsible for many of the differences we see between different cell types. Particularly in cancer, the chromatin structure of the cells can go wrong allowing the cells to manage their own DNA without it being under control. I look at several of the proteins and modifications involved in the packaging of DNA. In my research, I use purified chromatin proteins in particular those in complex with dPIAS to establish which interactions depend on post translational modifications. Understanding chromatin establishment and maintenance is critical for specifying and maintaining distinct cell types. By understanding fundamental cell biology, we can develop cancer therapeutics or control directed differentiation for cell therapies production.

2ND YEAR STUDENTS

Selma Gulyurtlu, University of St Andrews.
Myotonic Dystrophy: The disease with the undefined mechanism.
Dr Judith E Sleeman, Dr Alan R Prescott.

Myotonic Dystrophy Type 1 (DM1 or Steinert's Disease) is a condition that targets every system in the body, and has a prevalence of 1:20 000 people affected globally. Specifically, it is a genetic condition that initiates its negative effects at a cellular level. Within the cell, a modified genetic code results in incorrect localisation of proteins, which disturbs their normal function. This then translates to Heart problems, Cataracts, Muscle wasting, Insulin resistance, and more, with the highest fatality rate being respiratory failure. However, overall it is unclear how the underlying genetic defect leads to these symptoms. Thus, how can one find a cure to DM1, or alleviate symptoms if one doesn't know how it works exactly? This project aims to look at protein localisation within the cell in a lot more detail than previously. It incorporates ultrastructural observation, which includes looking at diseased cells under the electron microscope. Doing this, one can observe their organisation at much higher magnification to unveil how exactly they are organised. By doing this we can look for changes in protein localisation and cellular structures that are associated with the disease. This is important because it establishes the exact role of these proteins in disease. This is imperative to make research translational, as deciphering the role will suggest which targets to develop and employ at a clinical level.

Jacob Hargreaves, University of Aberdeen.
The Fungal Soil Microbiome of South Georgia and the Falklands.
Prof Pieter van West, Prof Jim Prosser & Dr Paul Brickle.

Soil is host to a huge amount of microbial complexity, with a mosaic like pattern of different communities; each containing their own unique blend of species. Because of this complexity the exact nature and purpose of these communities is not fully understood. This is despite their importance in biogeochemical cycles, which affect agricultural and natural ecosystems. Major contributors to soils are fungi, they have critical roles in breaking down organic matter; a subgroup can also form symbiotic relationships with plants, known as mycorrhizae, which can increase plant productivity. The Falkland Islands and South Georgia represent isolated natural ecosystems with introduced herbivores such as sheep and reindeer. To investigate fungal diversity in these circumstances, soil samples have been collected from various sites and targeted metagenomics is being used to reveal the exact community composition. This is done by targeting a specific region that is common to the DNA of almost all fungi; so when this soil DNA (eDNA) is extracted the specific region can be amplified via a process called PCR. The resultant product is read via an Illumina next-generation sequencer.

The results of this will greatly expand our knowledge of fungal diversity in the locality of the Falklands and South Georgia. It also has applications further afield in bioremediation and agriculture giving this work importance on a regional as well as a global scale. Future work investigating these communities via a proteome approach is also being planned.

2ND YEAR STUDENTS

Richard Hassall, University of Aberdeen.
Understanding the influence of population structure on disease risk.
Sandra Telfer, Stuart Piertney and Xavier Lambin.

My research focuses on improving our ability to predict and manage the disease risk to humans from zoonotic pathogens (bacteria, viruses, fungi and parasites passed from animals to humans that cause disease in the humans). These pathogens are often able to persist for long periods of time within an animal population, forming a natural reservoir for these organisms, this can lead to more opportunities for a pathogen to be passed onto a human. Approximately 60% of pathogens that infect humans come from these reservoirs and the majority of these are transmitted by insects. Some well-known examples of zoonotic pathogens include Influenza, HIV, Ebola, Plague, Lyme disease and Salmonella. However, we still have a limited understanding of how pathogens behave in these natural reservoirs and the mechanisms that increase the likelihood of pathogens persisting and evolving.

To explore these mechanisms I am studying a group of bacteria, Bartonella, which infects water voles and field voles in the UK and is transmitted by insects. My research aims to understand how changes in the animal, insect and pathogen populations influence the ability of Bartonella to persist in these small rodent populations but also how these changes influence the ability of Bartonella to evolve. By understanding how these changes influence bacteria we can start to tease apart the processes within natural reservoirs that could lead to increased disease risk to humans from natural reservoirs of zoonotic pathogens.

Stephanie Laba, University of Dundee.
Understanding how the body combats fungal infections.
Simon Arthur, Matthias Trost, Gordon Brown.

Fungal infections are a vastly growing problem: Nearly 2 million people are killed by invasive fungal pathogens every year in hospitals, whilst recurrent superficial fungal infections will afflict 1 in 3 women during their lifetime. Though bacterial infections are well studied and understood with many treatments available to patients, there is comparatively very little research into fungal infections and study into how the human immune system fights off these pathogens, with few treatments available and antifungal resistance to these drugs an increasing problem.

My research is focused on how the immune system combats the fungal pathogen Candida albicans. C. albicans is an opportunistic pathogen which is the most common fungal pathogen found in the bloodstream of hospital patients, carrying with it a high death rate in these patients. My project will examine what events are triggered in macrophages, a type of immune cell, when they are infected with C. albicans and will explore what proteins within the cell are important for combatting and eliminating the fungal pathogen.

By identifying proteins of importance involved in the antifungal response of macrophages, we will increase the understanding of how the body fights off these pathogens. This could lead to the discovery of therapeutic targets, and so to new ways to help and possibly enhance the body's antifungal response, thus bettering a patient's chances against fungal infections.

2ND YEAR STUDENTS

Maiju Laurila, University of Dundee.
Discovering de-S-acylating enzymes in Arabidopsis.
Piers Hemsley and Paul Birch.

S-acylation is the only reversible lipid-based post-translational modification (PTM) of proteins. It involves the covalent attachment of fatty acyl chain to a cysteine residue through a thioester bond and is thought to play a similar role in cell signalling to phosphorylation. Acyl protein thioesterases, or APTs, are serine hydrolase enzymes that remove acyl groups. No APTs are known from plants and only a few have been identified in mammals.

By combining competitive activity-based protein profiling (cABPP) with a complementary click chemistry approach we are identifying serine hydrolases in plants that are sensitive to inhibitors of de-S-acylation. Type-I ROP small GTPases undergo cycles of activation state dependent S-acylation and de-S-acylation. The model Type-I ROP, ROP6, will therefore be used as a model system to characterise candidate APTs based on de-S-acylation of ROP6.

Identification of APTs in plants will expand our knowledge of how this relatively little studied PTM is regulated. In the future we aim to define the dynamically S-acylated proteome to allow us to begin to investigate how S-acylation regulates plant protein function.

Abigail Lee, University of St Andrews.
Visual Processing of 3D motion.
Julie Harris and Justin Ales

Motion is a constant feature in our lives, whether it is our own motion as we walk around or the motion of objects around us in the world. In most situations when we see objects moving in the world they move in three dimensions, rather than in two dimensions as on a screen. For many animals, being able to see a predator moving towards them may mean the difference between life and death. Humans too rely heavily on their ability to see 3D motion to survive, but while 2D motion perception has been extensively studied, less is known about how we perceive motion in the third dimension. 3D motion looks very different to 2D motion on the retina of the eye and there are multiple types of visual information that we can use to perceive it. I am interested in how we combine these different types of visual information to see 3D motion, as well as the differences between how we perceive 2D and 3D motion. To investigate this, human participants make judgements about the motion of stimuli containing different visual information on a screen. If these judgements alter significantly it may indicate which type of visual motion information is used most when viewing motion in the real world. This may have implications for people who are unable to see motion, which can occur following stroke and brain damage. This work may also affect how virtual reality systems are developed to make them as realistic as possible.

2ND YEAR STUDENTS

Alasdair Leeson-Payne, University of Aberdeen.
The role of γ-synuclein in adipocyte function and energy expenditure.
Dr Justin Rochford.

Obesity has now escalated into a worldwide health epidemic bringing with it an increase in cases of associated diseases and an increased strain on the healthcare infrastructure. The demand for an effective and long-term treatment for obesity has become imperative. The overarching aim of our research is to investigate the role of adipose tissue (fat), including its development and function, to identify effective targets for the treatment of obesity and other diseases linked to the dysfunction of adipose tissue. Γ-synuclein (principally known as a neuropeptide) is a protein highly expressed in white adipose tissue and which is increased in obesity. Recent publications from our group identified that the γ-synuclein–null mouse model was partially protected from high-fat diet (HFD) induced obesity as well as reducing some of the associated metabolic complications. Evidence indicates γ-synuclein negatively affects the processes of lipolysis (fat breakdown) and energy expenditure in the adipocyte cell. The mechanisms through which γ-synuclein is involved or regulates these mechanisms is unclear and our research focuses on elucidating γ-synuclein's role. Our primary objectives are to identify how γ-synuclein affects lipolysis, mitochondrial function and energy expenditure in adipocytes with the ultimate aim to identify unique targets for treatment.

Aoife Leonard, University of Aberdeen.
Niche Evolution of a crop pest under climate change.
Dr Lesley Lancaster, Prof. Michael Ritchie & Prof. Jörgen Ripa.

Climates are currently changing at an unprecedented rate, and many organisms are responding to these changes with dramatic range shifts involving evolutionary responses. They evolve rapidly and quickly disperse into available niches, often posing new threats to food security (as crop or stored-food pests), human and animal welfare (as disease vectors), and affecting overall ecosystem function.

The mechanisms of evolution and range shift under rapidly changing climates remain poorly understood. One question relates to the order of trait divergence. In a model of α-niche priority for population divergence, organisms first evolve traits related to their within-community niche (i.e., the α-niche), such as alternative patterns of resource-utilization, species-interaction, and microhabitat use. New ways of interacting with their local habitat may then facilitate range expansion by providing new ways to overcome prior geographic limitations. Conversely, under β-niche priority, environmental change induces range shifts (i.e., adaptation to novel habitats and locales, the β-niche) prior to or in lieu of local, α-niche differentiation. β-priority implies limited scope for fine-scale local adaptation, which may limit the success of organisms that have nowhere suitable to go as climates change, while α-priority suggests that climate change may trigger successful invasions and adaptive radiations.

We aim to investigate conditions under which these alternative niche evolution scenarios may occur, using experimental evolution under quasi-natural selection in seed beetles, a major pest on stored legumes and grains worldwide. In addition to undergoing geographic range expansions worldwide, the species exhibits frequent evolutionary transitions among resources bringing highly negative economic impacts.

2ND YEAR STUDENTS

Oscar Maclean, University of Edinburgh.
Gene and genome evolution in malaria parasites (Plasmodium species).

Michael McDonald, University of Edinburgh.
Using synthetic ecology to optimise methanogenic consortia for anaerobic digestion.
Andrew Free.

2ND YEAR STUDENTS

Dario Miroli, University of Edinburgh.
Controlling gene expression in Escherichia coli through mechanical compression.
Dr Teuta Pilizota, Dr Meriem El Karoui.

Bacteria regulate the expression of their genome in response to a wide range of environmental conditions, including temperature, external osmolarity, presence or absence of certain chemical species and density of neighbouring cells. However, and in contrast to mammalian cells, there remain relatively few examples of changes in bacterial gene expression directly in response to external mechanical forces. The aim of the project is to achieve genetic expression of a fluorescent reporter protein in response to controlled mechanical compression, by utilising part of E. coli's osmoregulatory network. To this end we have developed a custom microscopy and microfluidic platform that allows us to control the application of mechanical force to single E. coli's cells simultaneously with imaging. Using the platform and the reporter fluorescent protein, expressed both constitutively on the chromosome and on a plasmid, we investigate the link between mechanical forces and gene expression, with a view to developing a whole cell mechanical force biosensor. It is hoped that ultimately this whole cell biosensor will lead to the development of smart biological materials such as self-healing concretes or novel drug delivery systems.

Amy Molotoks, University of Aberdeen.
Impact of land use change on biodiversity and food security.
Professor Pete Smith and Professor Terence P. Dawson.

One of the greatest challenges of the 21st century is to meet society's growing food needs whilst reducing the environmental impact of agriculture and one of the ways in which to meet future demands is by agricultural expansion. My research area involves using future global projections of cropland expansion for the model IMAGE 3.0 under various socio-economic scenarios including continuation of current trends. The impacts of this land use change on biodiversity have been examined including biodiversity hotspots as defined by Conservation International as well as AZE sites, containing endangered and critically endangered species as identified by the IUCN Red List. By highlighting areas particularly at risk, policy can be developed to protect important habitats and prevent future biodiversity loss.

The impacts on other ecosystem services will also be quantified which involves using the Harmonized World Soil Database to examine impacts of land use change on soil carbon. High resolution datasets on global forests will be used as well to determine how cropland expansion effects carbon storage in above ground biomass.

Furthermore, the global FEED-ME model informed by FAO statistics and nutritional demand will examine the various socio-economic scenarios to show how changes in agricultural land area, climate and population effect food security and the proportion of undernourished per country

2ND YEAR STUDENTS

Benjamin Moore, University of Edinburgh.
Derivation of bovine macrophages from induced pluripotent stem cells as a novel tool for understanding host-pathogen interactions.
Elizabeth Glass, Xavier Donadeu.

Sarah Morson, University of Edinburgh.
Imaging Dynamic Cellular Behaviour in the Developing Brain
Thomas Pratt and David J. Price

The process of the brain developing from a single fertilised cell to the most sophisticated known organ requires complex processes occurring at precise time points. An area of particular interest for researchers is cortex development. In order for generation of optimal cortical architecture and size, individual cells within a population must behave heterogeneously. It is well established that instructions for development are transmitted to cells by signalling molecules, they are global signals secreted to large groups of cells. However population dynamics and single cell behaviours differ with individual cells exposed to the same signalling molecules exhibiting different responses. In order to understand how the complete system of neural development works we must also understand how cells behave individually.

This project focuses on the Erk signalling cascade, a signalling pathway critical to development and its dysregulation is implicated in a range of neurodevelopmental disorders. Many aspects of Erk activation impact cell fate, particularly the time period of activation, a period of minutes rather than days. As the dynamics of Erk activation affect cell fate, understanding its activation kinetics is essential to understanding its role. We are utilising novel reporters of Erk activation to investigate the kinetics of Erk in cortical progenitors using live imaging techniques. Elucidating this will provide much novel information into the importance of Erk activation in the developing cortex.

2ND YEAR STUDENTS

Emily Parr, University of Edinburgh.
Molecular characterisation of bacterium-macrophage interactions: immune evasion, host-specificity and therapeutic potential.
David Hume, J. Ross Fitzerald.

Paul Rouse, University of Edinburgh.
The Application of Tissue Engineering to Develop an in vitro Thymus.
Clare Blackburn.

Following bone marrow transplantation, the T-cell component of a patient's haematopoietic system takes far longer to re-establish itself than other cell types. In some, T-cell reconstitution never occurs leading to AIDs-like symptoms for the rest of the patient's life. The thymus is the organ responsible for both initial generation of T-cells during development and reconstitution following surgery. This project aims to provide a platform for cellular replacement therapies to improve thymic rebound post-surgery.

Our group has previously described a thymic epithelial precursor cell (TEPC) population capable of generating functional thymi when engrafted under the kidney capsule of recipient mice. Generated thymi recapitulated the branching 3D network of thymic epithelial cells (TEC), which are broadly defined into medullary and cortical regions, necessary to produce T-cells within the native thymus. More recently, our group showed enforcing Foxn1 expression reprograms murine embryonic fibroblasts (MEFs) into induced thymic epithelial cells (iTEC) that possess the same capability to self-organise into functional thymi when engrafted into recipient mice.

This project aims to establish in vitro culture conditions for TEPC and iTEC in 2- and 3D. Presently, this project has identified candidate artificial matrices for the 2D culture of TEPC and iTEC and produced methodology to generate fully patterned 3D organoids in vitro using Matrigel. The next step is to assess how candidate artificial matrices affect TEPC and iTEC in regards to the maintenance of TEC phenotype, functionality and capacity for self-organisation in vitro across both 2D and 3D platforms.

2ND YEAR STUDENTS

Nicholas Senn, University of Aberdeen.
Development of advanced diffusion MRI for non-invasive tissue microstructure profiling.
Jiabao He and David Lurie.

Tissue microstructure underpins tissue functional health and is often affected in disease processes. Diffusion-weighted imaging (DWI) probes tissue microstructure by assessing the water movement after interaction with tissue membranes, allowing the visualisation of high cell density tissue regions non-invasively. The effects of cell boundaries on impeding water free movement can be assessed by diffusion kurtosis imaging (DKI), since kurtosis is an indicator of deviation from random movement. A comprehensive tissue microstructure picture can be obtained from q-space imaging (QSI), through the measurement of full water movement pattern. However, these methods are often limited to preclinical environment on small samples imposing special demands on hardware and long scan time. We therefore translated these methods to human scanner and compared QSI, DWI and DKI in whole breast tumours excised from patients.

Sixteen female breast cancer patients were enrolled with images acquired across the centre of the tumour. The water diffusion root-mean-square displacement (RMSD) maps were computed for each model. All tumour voxels were pooled to allow direct voxel comparison for correlation analysis to assess model agreement. Significant linear correlations (P values <0.005) were found for RMSD comparison between QSI against DWI (R, 0.844) and against DKI (R, 0.933). The strength of correlations for QSI against DKI compared to QSI against DWI implies the heavy involvement of tissue membrane within the tumour.

These results provide a springboard for further clinical translation of QSI in breast cancer where improved profiling of diffusion pattern in-vivo may have impact on measuring treatment response, diagnosis and prognosis.

Andrew Shaw, University of Dundee.
Investigation of regulation and downstream signalling of PINK1 kinase.
Miratul Muqit

2ND YEAR STUDENTS

Greg Sutton, University of Dundee.
Genome scale decoding of post-transcriptional modulators in African Trypanosomes.
Prof. David Horn.

The protozoan Trypanosoma brucei is an early-branching eukaryote and a causative agent of human and livestock disease in sub-Saharan Africa. The processes underlying T. brucei gene expression remain uncharacterized and could influence future drug development. Firstly, a genome-wide RNAi screen has indicated disruption of a putative chromatin remodelling complex as a mechanism of resistance to compounds from the experimental BA02 and BA05 chemical series. Secondly, there is a dearth of introns in T. brucei. Only two transcripts for a Poly(A) polymerase and a DEAD/H helicase contain an intron. The role of either intron remains elusive. In this regard, this project aimed to (i) validate a putative chromatin remodelling protein defect as a mechanism of resistance to BA02, and BA05 compounds and (ii) understand what role introns play in T. brucei. To follow up on this, RNAi constructs were generated to deplete the levels of two proteins: a putative CW-Zinc Finger protein and a putative SET-domain protein. Knockdown of the SET-domain protein transcript resulted in BA05 drug resistance while knockdown of the CW-Zinc Finger protein was lethal. Immunofluorescence analysis indicated the CW-Zinc Finger protein localises to the nucleus. Interrogation of examined genomes demonstrated that both introns are conserved throughout trypanosomatids. CRISPR/Cas9 was employed to edit the DNA of each intron. Cas9 constructs were generated, and transfected cells showed robust regulation of Cas9, however, no genome editing was detected. This study identified the loss of a chromatin remodelling protein in drug resistance and established the conservation of introns throughout trypanosomatids.

Hamish Todd, University of Edinburgh.
Applications of VR to structural biology research and teaching.
Andrew Goryachev, Taku Komura and Jeyaprasha Arundalam.

Protein structures are intricate three-dimensional shapes, and the specific placement of atoms inside them can have deep implications for their function. As a result, this structural information is difficult to directly work with using traditional tools. Powerpoint presentations on proteins may show a large number of images of them, but it is not easy for the audience to put these images together into an internal picture. And enormous amounts of structural biologists' time is consumed by turning electron density maps into usable molecular models, because the 3D graphics-enabled program "Coot", which all structural biologists use for the task, can only use a 2D screen, and 2D mouse input.

VR hardware offers the opportunity to solve these problems, and so we have been developing VR software. With "VRCoot" we expect to be able to hugely speed up the process of using Coot in a way that is accessible to a large number of scientists. And with our VR presentation techniques, we hope to create a new and intuitive way to convey information about protein structures, that makes it easier to create presentations on proteins and more enjoyable to watch them.

2ND YEAR STUDENTS

Matilda Toivakka, University of Edinburgh.
The role of microRNAs and their targets in T-cell responses.
Prof Rose Zamoyska and Dr Amy Buck.

The immune system exists to protect the body from infection and disease, however when dysregulated it can be the cause of disease. Such is the case in autoimmune disease, where healthy tissues are targeted by the immune system. In order to treat these disorders, it is important to understand the underlying molecular mechanisms that cause the inappropriate activation of self-reactive immune cells. T cells are a type of immune cell that have a key role in regulating immune responses and thus are important for the pathology of many autoimmune diseases. T cell activation and differentiation is regulated in many different ways, but my project focuses on the role of a particular group of molecules called microRNAs (miRNAs). miRNAs are small intracellular molecules that function by binding to and inhibiting their target messenger RNAs (mRNAs), which code for proteins and thus miRNAs influence which proteins a cell produces. Therefore to understand the role of miRNAs in T cell activation, we need to know exactly which mRNAs they regulate. To do this we are using a novel biochemical method in which we can physically join the miRNAs in the cell with their target mRNAs and then identify both using sequencing. Gaining information about miRNA targets will improve our knowledge of the mechanism of action of miRNAs as well as the signalling pathways surrounding T cell activation in health and in disease. Additionally miRNAs may be useful targets for therapeutic intervention in disease.

Fatima Ulhuq, University of Dundee.
Characterisation of a novel secreted virulence protein from Staphylococcus aureus.
Tracy Palmer.

The Gram-positive bacterium, Staphylococcus aureus, is a major pathogen of humans and animals. In humans it is a leading cause of community and hospital acquired infections and is associated with life-threatening diseases such as pneumonia, meningitis, endocarditis, toxic shock syndrome, bacteraemia, and sepsis. It costs the UK dairy industry millions of pounds each year in lost milk production as it is the leading cause of mastitis in dairy herds. The organism is notorious for its ability to develop resistance to antibiotics, and is one of the seven bacterial species highlighted by the World Health Organisation and the O'Neill report as being of critical antimicrobial resistance concern. Bacterial virulence factors that directly interact with the host must be secreted from the bacterial cytoplasm where they are made. Protein secretion systems are therefore critical to the success of all bacterial pathogens. We and others have shown that the Ess (Type VII) protein secretion system plays a critical role in the ability of S. aureus to cause disease. The aim of my project is to characterise a novel secreted protein (TspA) of the Type VII secretion system, and elucidate its role in virulence. Understanding how bacteria cause disease is critical to the development of new antibacterial compounds. Moreover, proteins that are secreted during infection may also provide opportunities for vaccine design.

2ND YEAR STUDENTS

Sally Vanden-Hehir, University of Edinburgh.
New Tools for Visualising Nanoparticle Drug Delivery for Healthy Remyelination.
Prof Anna Williams, Prof Valerie Brunton & Dr Alison Hulme.

Biodegradable polymeric nanoparticles (NPs) are becoming increasingly popular for targeted drug delivery. Recent work in the Williams group (Scottish Centre for Regenerative Medicine), 1 has shown that NPs can be used for drug delivery to the central nervous system to promote remyelination in multiple sclerosis disease models. However, as yet no direct link between the observed biological effect and nanoparticle delivery has been established.

The most commonly used degradable polymer is poly lactide-co-glycolide (PLGA) which is an FDA approved polyester which degrades slowly in vivo via hydrolysis to give sustained drug release. Functionalisation of PLGA NPs with antibodies allows targeting of the NPs to specific cells in the brain. PLGA NPs loaded with the protein leukaemia inhibitory factor have been shown to promote remyelination by increasing the rate of maturation of oligodendrocyte precursor cells to oligodendrocytes, which are responsible for producing myelin.

Raman spectroscopy provides near label free imaging conditions and is sub-optical in resolution. Introducing a bio-orthogonal label into the PLGA will allow the NPs to be visualised via Raman spectroscopy, enabling them to be tracked for the first time and questions about their uptake, distribution and degradation to be answered. To allow incorporation of the bio-orthogonal label, the polymer PLGA has been synthesised and fabricated into NPs using the both the emulsion-evaporation and nanoprecipitation methods. The PLGA was characterised by NMR, IR, Raman and SEC; and the NPs have been visualised by TEM. Double emulsion techniques have allowed the incorporation of BSA as a model protein, and we are currently investigating surface functionalisation.

Efrain Zarazua-Arvizu, The University of Edinburgh.
Engineering thermostable nanocompartments for protein production and enhanced enzyme activity.
Jon Marles-Wright, Louise Horsfall, Janice Bramham.

The production of recombinant proteins plays a key role in the biotechnology industry. Sundry economically important biochemical compounds; i.e., drugs, antibiotics and enzymes are produced as recombinant proteins. Consequently, several technologies have been developed to enhance protein production in common industrial hosts. However, there are still various challenges to achieving high production levels of toxic proteins, or to control the production of toxic intermediate metabolites within the host, as well as the maintenance of stable proteins by ensuring their appropriate folding in the host. Furthermore, separation of these protein products can be challenging. The bacterial nanocompartments, also called encapsulins, are produced by some species of bacteria and archaea and possess characteristics that can potentially overcome the current challenges of recombinant production of proteins. Encapsulins are simple icosahedral protein shells that encapsulate single enzyme species to protect the cell from oxidative damage. Nanocompartments are beneficial to cells because they increase the local concentration of enzymes, discriminate access of molecules, ease substrate transfer and enclose toxic products. The main objective of this project is to engineer bacterial nanocompartments to create a platform to encapsulate high-value proteins, in order to increase their production and to enhance enzyme activity for downstream applications by the utilisation of synthetic biology approaches based on Modular DNA assembly methods

3RD YEAR STUDENTS

Omar Alfituri, University of Edinburgh.
Dissecting the lymphatic invasion and systemic dissemination by African trypanosomes.
Prof. Neil Mabbott and Dr Liam Morrison.

African trypanosomes are single-celled extracellular protozoan parasites that are transmitted via the tsetse fly vector. Trypanosoma brucei subspecies cause trypanosomiasis in humans and animals across sub-Saharan Africa, inflicting substantial disease and economic strain, as 20 million new cattle are infected per annum. The impact of disease results in a $4.5 billion loss to the region annually, significantly affecting the whole society. This is due to a loss of livestock and their productivity as well as the costs incurred from preventative measures (e.g. fly nets) and expensive and out-dated treatments which can produce severely adverse effects. This impact also stems from lack of work due to disease burden and disability.

Mammalian infection begins when the tsetse fly injects trypanosomes into the skin dermis. The parasites invade the circulatory and lymphatic systems, reaching the draining lymph nodes before disseminating systemically. How this occurs is not known.

Through investigating the host-pathogen interactions occurring during these early skin and lymph node stages of infection we may be able to identify the molecular and cellular mechanisms that influence the establishment of African trypanosome infection in the skin and their subsequent systemic dissemination. The aim being to aid in the development of novel approaches to block disease transmission. Thus helping to alleviate the economic strain on local economies, the livestock industry and animal healthcare, whilst bolstering both human and veterinary medicines.

John Hunter Allan, University of Dundee.
Signalling and regulation of bacterial virulence.
Frank Sargent.

3RD YEAR STUDENTS

Stevie Bain, University of Edinburgh.
Parent-of-origin specific genomic exclusion in insects.

Emma Louise Bradford, University of Aberdeen.
Relationships between Deformed wing virus, European Honeybees and Varroa destructor?
Dr Alan Bowman and Dr Ewan Campbell

The European Honeybee (Apis mellifera) is the world's most economically important pollinator, making them critically important to global food production. Worryingly, a honeybee health crisis has developed in recent years, which is threatening both honeybee populations and global food security. These recent health threats can be linked to the recent global spread of the invasive parasitic mite, Varroa destructor. This parasitic mite is having a devastating effect on honeybee colonies due to its ability to transmit several major honeybee viruses. One such virus is Deformed wing virus (DWV), which is having an alarming effect on UK and European bees. This project aims to understand the complex relation that exists between honeybees, Varroa and DWV. DWV is an RNA virus that exists as many closely related variants of differing pathogenicity. Viral transmission through Varroa has altered this viral landscape resulting in an increased prevalence of the more pathogenic variant (DWV-B). Understanding DWV variant composition within honeybee colonies is of great importance to improve our knowledge of this globally important viral infection. This project, with the aid of a newly designed viral assay will study A). Varroa viral transmission, B.) Pathogen spill over to other pollinators and C.) Viral dynamics within colonies. This understanding of DWV infections is crucial as currently there are no treatments available, with most efforts aimed at Varroa management. While this project is not aiming to develop a viral treatment, it is hoped the information gained may be able to inform future management practices in regard to DWV Varroa interactions.

3RD YEAR STUDENTS

Lindsey Caldwell, University of Edinburgh.
Regeneration of dopaminergic neurons in the adult zebrafish brain.
Prof. Catherina Becker and Dr. Thomas Becker.

Parkinson's disease affects 1 in 500 people and there is currently no cure available. As with other neurodegenerative diseases, Parkinson's disease presents a significant financial, social, and economic burden to society.

In Parkinson's disease, dopaminergic neurons of the substantia nigra are progressively lost and not replaced. Unlike mammals, zebrafish are able to functionally regenerate their central nervous system. When dopaminergic neurons are ablated by injection of the selective catecholaminergic neurotoxin 6-hydroxydopamine (6OHDA), progenitor cells around the diencephalic ventricle proliferate and generate new dopaminergic neurons to replace those which have been lost. We aim to uncover the molecular mechanisms underlying this cell replacement.

It has been suggested that neurogenesis may be controlled in a cell type specific manner, with dopamine itself regulating the number of dopaminergic neurons. To test this hypothesis, we injected the dopamine receptor antagonist haloperidol to mimic a loss of dopaminergic neurons. However, we found no difference in the number of proliferating progenitor cells.

Activation of immune cells has been shown to promote neuroregeneration. We found injection of the inflammatory agent Zymosan A. causes a microglial reaction and successfully increases the number of proliferating progenitor cells, both with and without cell ablation. As microglia activation is sufficient to increase progenitor cell proliferation, we hypothesise that a molecular signal released by activated microglia stimulates progenitor cells to proliferate.

Ultimately, determining the signals by which zebrafish replenish their dopaminergic neurons may inform therapeutic approaches to cell replacement for people with Parkinson's disease.

Adam Clement, University of Edinburgh.
Identifying genetic interactions linked to gene expression in mammalian genomes.
James Prendergast and Neil Chue Hong.

Interactions between genetic variants may be a major underlying factor in explaining unsolved issues in genetics such as 'missing heritability' and the paradox as to why potentially harmful mutations are not removed rapidly from mammalian populations. Each human contains approximately 3-4 million single nucleotide polymorphisms (SNPs), thus detecting genetic interactions genome-wide is difficult due to the substantial computational and statistical burdens associated with this type of analysis. This project uses a new approach to identify these genetic interactions by studying allele-specific expression (ASE), which is where the allele on one chromosome is expressed to a different extent than the allele on the other chromosome. The basis for ASE is multifactorial because it may be the result of genetics, epigenetics, the environment or any combination of the three. By using novel bioinformatics techniques genetic variants associated with the extent of ASE have been identified, enabling the identification of interactions with the primary determinants of ASE at the corresponding genetic loci. The results show that a subset of coding variants show ASE (approximately 0.001%) and that nearby variants modify the extent of expression at these loci presenting with ASE. The relevance of these interactions to detecting the genetic loci linked to diseases and traits will subsequently be investigated. These findings impact a wide variety of societal institutions, from medicine to agriculture.

3RD YEAR STUDENTS

James Clugston, University of Edinburgh.
Exploring new approaches for conservation genomics of Cycas L. (Cycadaceae) in Australia.
Richard Milne, Gregory Kenicer and Nathalie Nagalingum

Many cycads exist as small populations, and so understanding the genetic variation in cycads is imperative for conserving the remaining populations and ensuring their survival. Genetic data plays a fundamental role to help conserve multiple genotypes and highlight populations with the greatest levels genetic diversity. Australia represents a significant biodiversity hotspot for cycads, yet their genetic diversity has yet to be explored in detail. The application of restriction associated DNA sequencing (RADseq) has been successfully applied to many non-model angiosperms for examining ancestral hybridisation, adaption and genomic differentiation in populations, as well as the role of natural species barriers. To understand the genetic diversity of wild cycad population in Australia we applied Next-generation sequencing and RADseq. We collected population level leaf samples were collected from wild populations of Cycas armstrongii, C. calcicola and C. maconochiei from the Northern Territory, Australia. By using RADseq we produced thousands of informative genome wide single nucleotide polymorphic loci, which were used to genotype individual in populations and highlight populations with the highest levels of genetic diversity. The RADseq data was used to: understand intraspecific and interspecific genetic variation in populations of species; identify putative hybrids; recognize populations of conservation priority; and determine if botanic garden collections successfully represent existing genetic diversity found in the wild.

Holly Corrigall, University of Aberdeen.
New tools to understand ribosome drop-off during translation.
Prof. Ian Stansfield and Dr. M Romano

One of the major classes of error in protein synthesis is ribosomal drop-off, which results in the production of truncated, incomplete proteins. Various mechanisms are believed to cause translational abandonment, many resulting from extended translational pausing at a given codon. To understand this process, a novel dicistronic reporter was constructed which expresses a translational fusion of red and green fluorescent protein genes in Saccharomyces cerevisiae. Ribosomal drop-off would be expected to shift the ratio between RFP and GFP, detectable using flow cytometry. The frequency of ribosome drop-off in response to translation error-inducing drugs was then tested, including geneticin (G418), an inhibitor of the elongation step of protein synthesis. Unexpectedly, growth in high concentrations of geneticin created two populations of cells, those in which red-green fusion proteins were still expressed (32% of population) and those in which only red protein was detected (62% of population). The latter suggests the existence of a population of cells exhibiting very high frequency translational drop-off, generating cells in which only RFP was detectable. This dual population effect was not observed when cells that were treated with two other elongation inhibitors, paromomycin and cycloheximide. The significance of these results will be discussed, along with the results of a screen to identify sequences that drive increased drop-off frequencies in yeast.

3RD YEAR STUDENTS

Matthew Dale, University of Edinburgh.
Production of saponins in Saccharomyces cerevisiae.
Susan Rosser.

Saponins are plant natural products that show a range of biological activities, including immunostimulatory, antimicrobial and anticancer activities, as well possessing foaming and emulsifying properties. Saponins therefore show great promise across a range of sectors, including in medicine, agriculture and in home and personal care (HPC) products. To obtain saponins in high enough quantities and purity for commercial use, high efficiency and cost-effective means of production must be available. Existing production methods include extraction from the native plant and total chemical synthesis, both of which have many limitations that make them unsuitable for the production of complex metabolites such as saponins. An alternative to these methods is microbial production, where biosynthetic pathways are heterologously expressed in a microorganism of choice. This approach has the potential to offer high yields and purities at low cost and from inexpensive carbon sources, such as glucose. This project aims to establish a platform for the production of saponins in the yeast Saccharomyces cerevisiae. Biosynthetic enzymes from a variety of saponin-producing plants will be expressed and their activities for the production of key saponins and saponin-precursors compared. To enhance saponin yields, native S. cerevisiae metabolism will be engineered to over-produce the saponin precursor 2,3-oxidosqualene. Such strains will facilitate the combinatorial biosynthesis of saponins, where biosynthetic enzymes from a variety of species are ‘mixed-and-matched’ to produce novel saponins not found in nature.

Estela Domingo Torres, University of Dundee.
Alternative Splicing and Nonsense Mediated Decay: Regulation of resistance gene expression in potato.
Ingo Hein, Craig Simpson and John W. S. Brown.

Plants had evolved systems to defend against pathogens and adapted pathogens deliver effector proteins inside host cells to suppress these defences. Effectors are detected by immune receptors; the cytoplasmic nucleotide binding leucine-rich repeat (NB-LRR) proteins, leading to effector-triggered immunity (ETI).

Using a NB-LRR gene enrichment and RenSeq, previous studies identified over 700 NB-LRR genes in potato. Most fall into two classes: the N-terminal toll/interleukin 1 receptor (TIR)-like domain (TNL) and N-terminal coiled-coil (CC) domain (CNL). TNLs show conserved gene nucleotide-binding domains and some show alternative splicing (AS). AS occurs in at least 60% of plant genes and is enriched in stress related genes, such as TNL and receptor-like kinase genes.

Dynamic changes in ratios of AS of TNL transcripts have been shown in tobacco and Arabidopsis to be essential for the plant response to infection. AS is also associated with mRNA stability through the activation of nonsense-mediated decay (NMD); a conserved RNA surveillance mechanism. NMD targets aberrantly spliced transcripts for degradation. These transcripts contain features that allow them to be recognised by the NMD machinery: for example, premature termination codons (PTCs) and long 3’ UTRs. In plant defence, some resistance genes such as TNLs are alternatively spliced such that transcripts are turned over by NMD. The hypothesis is that infection alters the efficiency of NMD leading to an increase in the alternatively spliced PTC-containing transcripts and thereby to efficient activation of the hypersensitive response.

We aim to understand a role for AS and NMD in the interaction between potato and P. infestans, by focusing specifically on the post-transcriptional regulation of NB-LRR genes. We have started to develop a method to analyse NMD in potato so that we can follow the changes and effects of AS on NB-LRR genes.

3RD YEAR STUDENTS

Alex Finney, Universiy of Dundee.
Exploring bacterial hydrogenases for biotechnology and biomedical applications.
Frank Sargent.

Amy Fraser, University of Edinburgh.
Determining the interacting network of TALPID3 through proteomic studies.
Megan G Davey and Michael J McGrew.

TALPID3 is a centrosomal protein that plays a role in centrosome orientation and migration, ciliogenesis and Hedgehog pathway signal transduction. The mutation found in the Talpid3 chicken flock is embryonic lethal and mutations in KIAA0586 (human ortholog) result in a range of ciliopathies including Joubert syndrome, Jeune syndrome and Short rib-polydactyly syndrome. TALPID3 is essential for normal cell function and life however, its precise function remains unresolved. We aim to uncover the functional consequences of the TALPID3 protein interacting network.

Using mass spectrometry, we are comparing the protein composition of isolated centrosomes from non-ciliated human Jurkat cells to the protein composition of isolated centrosomes from ciliated chicken Primordial Germ Cells (PGCs). Novel centrosome protein candidates are being validated through in situ hybridisation and CRISPR editing in the chick. Using PGCs derived from wildtype and talpid3 chicken embryos, quantitative proteomic analysis is being undertaken to compare the changes in levels of protein expression. This data will provide an insight into the proteins that interact with TALPID3 and help tease apart the TALPID3 interacting network, based on upregulation and downregulation of centrosome proteins and pathways.

Using proteomic approaches firstly to understand the composition of the centrosome in a chicken primary cell line and secondly to analyse TALPID3 protein interactions, we can begin to determine exactly how TALPID3 controls processes like centrosome length and orientation, alterations to the centriolar satellites and tissue polarity. This knowledge can further our understanding of the less severe phenotype seen in human patients compared to the Talpid3 chicken.

3RD YEAR STUDENTS

Kathryn Grant, University of Edinburgh.
Mechanically induced developmental plasticity in plants: Its mechanisms and application to sustainable agricultural improvement.
Dr Catherine Kidner.

Iain Hunter, University of Edinburgh.
The Molecular Mechanisms of Mechanosensation in Skeletal Muscle Proprioceptors.
Prof. Andrew Jarman, Prof. Douglas Armstrong, Dr. Guy Bewick.

Mechanosensation is the ability to perceive a mechanical stimulus like vibration or stretch. The link with vibration means that mechanosensation is necessary for hearing (sound waves are sensed as deflections in specialised nerve cells of the inner ear in humans). 1 in 6 people in the UK are hard of hearing and understanding the mechanisms of mechanosensation could reveal targets for treatment of hearing loss. The location, specialisation and fate of mechanosensitive cells of the ear makes studying them difficult, so we are using a simpler fruit fly (Drosophila) model of mechanosensation to understand general mechanisms that we can apply to the ear in future work. This Drosophila model is based on a specific nerve cell, the dbd neuron, which could behave similarly to the mammalian muscle stretch sensor, the muscle spindle. Our electrophysiology data suggests that the dbd neuron does behave similarly to the muscle spindle and that protein channels DmPiezo and TRPA1 may contribute to its activity. This data is, however, subject to limitations that we are working to overcome with optogenetic and calcium imaging techniques. Doing so could validate human equivalents of DmPiezo and TRPA1 as targets for treatment of hearing loss.

3RD YEAR STUDENTS

Bobby Innes, University of St. Andrews.
Understanding Multisensory Benefits in Response Times.
Dr. Thomas Otto, Dr. Dhanraj Vishwanath

We are constantly presented with sensory signals in multiple modalities. For instance, smartphones signal their users in the visual, auditory, and tactile modalities. Such devices also present signals in different sensory modalities simultaneously, e.g. a sound and flash together. Our response times (RTs) to these multisensory stimuli are faster than RTs to either of the component unisensory signals: this is a multisensory benefit. Is it possible to take advantage of these multisensory benefits to improve interactions with technology we use every day? One successful model of multisensory RT benefits offers two key principles for predicting their size: benefit size increases when RTs to the component unisensory signals are similar ('equal effectiveness'), and when these unisensory RTs are highly variable (variability rule). By better understanding how these two principles interact to produce the multisensory benefits observed, it is possible predict the size of the benefits for different signals and develop methods to further increase benefits. The aim of this project is to quantify sources of unisensory RT variability as (according to the variability rule) this is directly proportional to the benefit size. Sources of overall RT variability include, for example, the level of variability or 'noise' in the stimuli presented, changes in attentional state, or variability in the motor component of the response. Manipulating these sources will offer methods to improve multisensory RT benefits, which could lead to faster, better-tailored interactions with technology such as smartphone apps.

Kaja Kostanjevec, University of Aberdeen.
Building an artificial cornea: Modelling stem cell activity and cell migration in the eye.
Dr Silke Henkes.

3RD YEAR STUDENTS

Piera Marchetti, University of Edinburgh.
Redefining the tambjamine YP1 biosynthetic pathway.
Dominic Campopiano.

Tambjamine YP1 is an antimicrobial bipyrrole natural product produced by Pseudoalteromonas tunicata1. Its predicted biosynthetic pathway is encoded in an operon of 19 proteins, 12 of these with biosynthetic functions2. We present the first characterisation of three of these enzymes and their roles in the pathway.

Two of the predicted proteins are TamF, a chain length factor (CLF)-ketosynthase (KS) fusion and TamD, an unusual acyl carrier protein (ACP)-alpha oxoamine synthase (AOS) fusion. These enzymes are postulated to work together to produce the first bipyrrole intermediate, 4-hydroxy 2,2'-bipyrrole 5-methanol (HBM) via two Claisen-like condensations. In order to explore these reactions, the enzymes have been recombinantly expressed and combined with substrates or substrate mimics in vitro. A combination of mass spectrometry and HPLC data provide the first evidence that these enzymes synthesise the initial HBM bipyrrolic intermediate.

An enzyme in the Tam cluster with no previously assigned function is TamA, an unusual fusion of a fatty acid AMP ligase with a C-terminal ACP domain. Recombinant TamA is isolated with a bound C12 fatty acid adenylate, which is transferred to the ACP domain upon phosphopantetheinylation. We propose that this C12 fatty acid, covalently bound to the ACP domain, acts as a substrate for downstream enzymes as opposed to the currently accepted hypothesis that this is carried out by enzymes out with the cluster1.

As well as in vitro studies, we are working on solving the crystal structures of all three enzymes to provide more insight into their catalytic mechanism.

Lucas J. Morales Moya, University of Dundee.
Somitogenesis on a chip.
Kim Dale, Philip Murray.

3RD YEAR STUDENTS

Holly Rore, University of Aberdeen.
Production of Sertoli cell-like cells capable of inducing germ cell differentiation.
Professor Kevin Docherty and Dr Ryo Sekido.

Throughout life Sertoli cells maintain close contact with developing sperm and so are considered to take an active role in directing their production, the process of spermatogenesis. As a result, they are an important consideration when attempting to produce sperm in the lab. One potential source of Sertoli cells are pluripotent stem cells (PSCs) which can form a range of different cell types. Here we adapt a protocol for the generation of intermediate mesoderm, the embryonic origin of Sertoli cells, and renal tissue

for the production of Sertoli cell-like cells (SCLCs). This method involves treating mouse PSCs for 2 days with small molecules CHIR99021 and TTNPB to recapitulate signalling pathways involved during development. This was followed by 6-8 days of treatment with signalling molecules BMP7 and FGF9, producing cells expressing genes characteristic of Sertoli cell identity and which localised to distinctive, elongated cell aggregates. Interestingly, these cells were not only capable of supporting primordial germ cell-like cell (PGCLC) survival in co-culture, they were also able to induce PGCLC identity in epiblast-like cells (EpiLCs) within 4 days, the cell type from which germ cells derive. Promisingly, this was without the need for external signalling factors or a 3D-cell matrix, but could be enhanced with the addition of 2% FBS and testosterone. These findings provide a basis for further examination of long-term co-culture, the potential role of cells produced alongside SCLCs and the nature of the germ cells produced. With time, these methods could be attempted using human PSCs and could have implications for the treatment of human infertility.

Andrew C. Runcie, University of Dundee.
Optimising a 'Bump-&-Hole' Approach for Selective BET Bromodomain Inhibition .
Professor Alessio Cuilli.

In the last several years increasing attention has been paid to the BET (bromodomain and extra-terminal) protein family – BRD2, BRD3, BRD4 and BRDT – as therapeutic targets for cancers, cardiovascular disease, sepsis and more. These proteins are epigenetic readers that detect chemical modifications to chromatin and regulate the expression of genes from DNA, using two bromodomains that recognise acetyl-lysine residues. Many inhibitors of BET bromodomains have been developed and several are currently in clinical trials. Unfortunately, however, these inhibitors are 'pan-selective' and inhibit all BET bromodomains equally, increasing the likelihood of adverse side-effects when used therapeutically and limiting our ability to study individual BET proteins. In the Ciulli lab we are working to implement a 'bump-&-hole' system which will allow us to target specific BET bromodomains for chemical inhibition. In this bump-&-hole system we introduce a mutation to the protein of interest and then modify existing inhibitors to make them bind only mutated proteins. We have previously done this in BET bromodomains with a leucine/alanine mutation and a JQ1-related benzodiazepine scaffold with an ethyl bump, and are now working to optimise this system. Once this system is implemented in cell-line and animal models we will be able to chemically study individual BET bromodomains. The exact roles and functions of the different BET proteins can then be investigated and those most important to diseases or likely to cause adverse effects can be identified. This information can then be used to develop the next generation of therapeutic BET inhibitors.

3RD YEAR STUDENTS

Ben Rutter, University of Aberdeen.
Exploring & exploiting the biosynthesis of myriocin, a potent fungal metabolite.
Dr Alex Brand, Prof Dom Campopiano.

Background: Myriocin is a secondary metabolite produced by at least 4 fungal species of the Hypocreales order, including Isaria sinclairii and Mycelia sterilia. A potent immunosuppressant and inhibitor of sphingosine biosynthesis, Myriocin has been exploited in cell biology studies since its discovery in 1972, but its structural simplicity permitted its development as Fingolimod, the first licensed oral treatment for multiple sclerosis. Our aim is to elucidate the biosynthetic pathway of myriocin as a potential source of bioactive intermediates and/or enzymes with biotech applications.

Results: Serine Palmitoyl Transferase (SPT) inhibition assays and LC-MS analysis of fungal growth supernatants detected maximum myriocin biosynthesis at 23 days at 37 °C. De novo genome sequencing of I. sinclairii and M. sterilia showed genome sizes of 24.89 Mb (N50 of 53.167 Kb) and 33.07 Mb (N50 of 66.951 Kb), respectively. We have also identified 24 secondary metabolite gene clusters in I. sinclairii and 20 in M. sterilia. A single gene cluster was conserved between the two fungi and encoded polyketide synthase (PKS) and pyridoxal phosphate (PLP) that are predicted to function early in the myriocin biosynthetic pathway. Targeted gene deletion is being used to validate the function of the identified myriocin gene cluster. Microscopy showed that, while M. sterilia grows only as multinucleate hyphae, I. sinclairii grows as hyphae in 37 °C, but as mononucleate yeast at 30 °C, an ideal morphology for genetic manipulation.

Conclusions: These are the first genome sequences to be generated for myriocin producing fungi. The discovery that the two fungi harbour 44 secondary metabolite gene clusters between them but share only one suggests that their lifestyles differ substantially. In the longer-term, further investigation of these gene clusters may reveal further bioactive compounds of pharmacological interest.

David J Walker, University of St Andrews.
Developmental programming of neuroendocrine and immune responses: implications for ageing.
Susan D Healy and Karen A Spencer

Developmental stress has significant and often permanent impacts on many biological functions, including stress and immune responses. Alterations of these responses affect the activity of regulatory mechanisms in the brain, such as the hypothalamic pituitary adrenal (HPA) axis and the neuroimmune response by microglia, which can influence phenotypic traits that affect long-term health. Recent evidence, on the other hand, suggests that developmental stress may program physiological changes that could prepare an individual to cope better with future stressful conditions.

To test this hypothesis, in my PhD I am investigating the long-term effects of developmental stress on HPA axis and immune function. Using an avian model system, the Japanese quail (Coturnix japonica), I have shown that post-natal stress induces changes in microglia number and reduced anti-inflammatory cytokine gene expression. I will explore how stress exposure during development and adulthood interact to influence cellular apoptosis and neurogenesis in the adult quail brain (9 and 24 months). Finally, I plan to use transcriptomic techniques to determine whether pre-natal stress leads to long-term changes in spleen function to uncover genes and pathways that could potentially induce a stress-resilient phenotype.

A rise in the ageing population over the last century has resulted in significant increases in the number of people suffering from age-related diseases (e.g. Alzheimer's), leading to growing healthcare costs of worldwide social and economic importance. As developmental stress impacts both positively and negatively on these age-related diseases, my research will allow us to identify the cellular mechanisms that drive these age-related diseases so that they may be targeted therapeutically in order to increase the quality of life and reduce the socioeconomic impact of ageing.