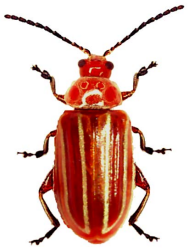

Peterhouse Biology Symposium 2023

Saturday 4th March 2023, Peterhouse Theatre

Justin Gerlach (Fellow) – **New but gone already – Madagascar's dry forest snails**
In 2019 I visited Anjajavy in north-western Madagascar. This area has small fragments of dry forest which have been lost from most of the island. It supports a remarkable fauna but the snails were almost completely unknown (2 species had been recorded previously). From the small collection I made and the more extensive material collected by two other people in 2003 and 2007 we recorded 102 species, of which 24 were new to science. Madagascar has an extraordinary diversity of snails (and everything else): with a land area twice that of Great Britain, it has 4.5 times as many described species, and we have just expanded that by a further 6%. Deforestation on Madagascar is dramatic and many forests only remain as tiny fragments; the species within them may be at critically low population levels. Three of the snails we recorded were found only as very old shells and may well be extinct already.

Danai Kontou (PhD) – **Tales from the deep: tracking the evolution of aquatic food webs in a changing world**
Focusing on zooplankton communities from Canadian Shield lakes and integrating genetics with palaeoecology, my research investigates the nature and repeatability of rapid adaptation in the wild. Using resting egg banks and microfossils from lake sediments we can learn how keystone species in lakes respond to environmental change and the introduction of invasive species. The aim is to offer insight into changing aquatic food web dynamics and how we can best manage and protect vulnerable lake ecosystems in the future.

Emily Naden (II Biochemistry) – **Staying alert: Investigating impaired hypoglycaemia awareness**
Hypoglycaemia associated autonomic failure (HAAF) affects ~25% of diabetic patients undergoing insulin treatment. This increases the risk of severe hypoglycaemia by 6-fold, which involves the induction of a coma and can lead to death if untreated. The mechanisms underlying HAAF are not well understood, partly due to the lack of a standard HAAF mouse model. In this talk I will discuss what we know about HAAF, the development of a standard HAAF mouse model and how this is being used to increase our understanding of HAAF with the aim of informing potential treatments.

Wes Robertson (Research Associate) – **Turning cells into living factories of the future**
Using the genetic code to synthesize drug-like molecules presents significant advantages over traditional chemistry based methods, namely programmability by DNA and evolvability within the cell. To adapt the biosynthetic machinery of cells to accommodate more chemical diversity, we generated a synthetic bacteria with an expanded genetic code that adds three more available building blocks for protein synthesis. To do this, we assembled a bespoke *E. coli* genome in which two sense codons and a stop codon, and the cognate transfer RNAs (tRNAs) and release factor that normally decode these codons, have been removed and then reassigned to non-canonical amino acids - we call these Syn61 cells. As a proof of principle for the DNA-encoded synthesis of drug-like molecules, we genetically encoded the synthesis of non-natural cyclic peptides. Using Syn61-derived cells, we programmed the biosynthesis of diverse non-natural macrocyclic peptides, each containing two non-canonical amino acids, and we then further increase chemical diversity by adding hydroxy acids for the encoded synthesis of non-natural depsipeptide macrocycles. This cell-based synthesis of diverse, non-canonical macrocycles sets the stage for their directed evolution for novel functions.

Sarah Bull (II Zoology) – **Rewilding in a changing world: Improving breeding success in a population of rewilded Giant Tortoises**

At the centre of my research interests is how our understanding of the behaviour and population dynamics of keystone species can drive restoration objectives. This presentation discusses the results of a two-month study on Cousine Island in Seychelles, studying a population of rewilded Giant Tortoises to identify causes of breeding failure. It will explore the interaction between social and ecological dynamics in tortoise populations and demonstrate how our understanding of these systems can support successful conservation strategies, especially as we move into a generation of immense environmental change.

Fani Memi (Research Associate) - **Mapping the tissue architecture of Glioblastoma Multiforme using Spatial Transcriptomics**

Anirudh Krishnakumar (II BBS) – **Tissue engineering approaches in cardiovascular applications and the role of proteomics**

Tissue engineering approaches in a cardiovascular setting have been focussed on "decellularisation", primarily involving 1% SDS, as the primary method of creating xenogeneic bioscaffolds. However, issues regarding immune rejection, due to presence of residual antigens, and gross morphological disruption have led to the development of a stepwise solubilisation technique by Griffiths et. al (2013) known as Antigen Removal. Here, we discuss the current progress of using the AR paradigm in valvular and vascular graft applications and the emerging need for proteomic analysis of AR scaffolds. The first project showed the efficacy of the method in preserving an intact extracellular matrix (ECM) in Bovine Pericardium and also in enabling Human Mesenchymal Stem Cell (HMSCs) migration in the z-direction using immunofluorescence assays. The second project involved bioreactor and cell-seeding experiments on bovine mesenteric arteries to test AR-treated scaffolds under physiological conditions. Moreover, histological analysis showed the presence of intimal hyperplasia in the arterial wall and hence prompts the need to reconsider choice of tissue for xenogeneic scaffolds. Following on from these experiments, the need to analyse the "niche properties" of AR-treated tissue is made evident and mass spectrometry was conducted to compare native and AR-treated bovine pericardium. Greater than 90% of proteins have been removed by the AR protocol. Further analysis of the proteomic data is required and can be significant in improving our understanding of the consequences of tissue engineering on cell-cell, cell-ECM and inflammatory mechanisms.

Charlotte Wright (PhD) – **Winging it: understanding genome instability in *Polyommatus***

Lepidoptera, the butterflies and moths, is a diverse order of insects with a largely conserved karyotype of 31 chromosomes, suggesting that the last common ancestor of the group also had 31. Against this background of karyotypic stasis, a subset of species display dramatic variation in patterns of genome and chromosome organisation. Recently, high-quality, chromosomal genome assemblies have been generated for over 200 species of Lepidoptera, enabling us to ask fundamental questions surrounding the processes that shape genome organisation in Lepidoptera. We used phylogenetically-aware analysis of conserved single-copy orthologs on chromosomes from 210 Lepidoptera and 4 Trichoptera (caddisflies; outgroup) to predict ancestral linkage group number and content across Lepidoptera. We find that lepidopteran chromosomes have remained remarkably stable with the vast majority of species having undergone none or just one fusion event. However, we identify nine independent lineages that have evaded the typical constraints of genome structure and undergone extensive reorganisation. These independent events allow us to identify two main modes in which genome reorganisation occurs: through numerous fission events; or through complex, fusion and fission events. Two instances of genome reorganisation in *Polyommatus*, also demonstrates that the Z chromosome is remarkably resistant to fragmentation. Together, these analyses demonstrate how chromosomally-contiguous genomes across Lepidoptera offer an unprecedented opportunity to explore the role of selective constraint in the evolution of genome structure.

Mia Messenger & Georgia Miller (II Zoology) – **Predatory Giant Tortoises**

In 2021, Gerlach & Zora published a paper on the predatory behaviour of giant tortoises in the Seychelles. They showed the first video evidence that giant tortoises deliberately hunt and attack birds. To further study this phenomenon, we spent 8 weeks on Fregate Island in the Seychelles observing the tortoises, the lesser noddy chicks and analysing faeces. We were interested in how widespread this behaviour is within the population, if

there are biases in which tortoises are likely to hunt and how successful attacks are. We found numerous cases of tortoises approaching chicks, attacking and even successfully catching and eating the chicks. Faecal analysis similarly shows that whilst it is occurring in various areas of the island, it is not particularly common and birds do not make up a large part of the tortoise diet. This behaviour is exciting with tortoises previously being described as strict vegetarians, the large overlap in giant tortoise and lesser noddy colonies on the island provides plenty of opportunity for this new phenomenon.

Georgia Miller (II Zoology) - **Does protein arginine methylation by PRMT5 play a role in cell proliferation and DNA replication?**

PRMT5 is the predominant type 2 protein arginine methyltransferase in cells, meaning it symmetrically dimethylates arginine residues in proteins. It has a huge variety of targets in cells affecting epigenetic regulation, DNA repair mechanisms, cell cycle progression and many more processes. Whilst many of the specific targets have been elucidated, the general effect of PRMT5 on cell proliferation and DNA replication remains unclear. Using EJ30 cells (human bladder carcinoma cells) and the specific inhibitor GSK591, I performed in vivo cell proliferation and DNA proliferation assays with BrdU incorporation. I have shown a dose-dependent decrease in cell proliferation with long incubation times of 3-5 days and that PRMT5 inhibition causes moderate inhibition of DNA replication with a higher proportion of cells in S phase but more of these cells have low BrdU incorporation. This suggests that the cells are stuck in S phase, likely though elongation inhibition.

Sebastian Ljung (II Physics) – **Exploring the regulation of domesticated transposons by KRAB zinc finger proteins in humans**

Transposons are DNA sequences with the capacity to replicate or reinsert themselves elsewhere in the genome. Initially they were considered purely antagonistic towards their host, but as usual the line between mutualism and parasitism is dynamic. KRAB zinc finger proteins (KZFPs) are known to help suppress and inhibit transposons, however Michael's lab has recently unveiled a more complex story of transposon domestication into relevant regulatory elements, with KZFPs as inhibitors. My presentation will be on my work creating an exploratory tool for finding the potential roles of discovered KZFPs and linking/applying to my previous internship on zygotic genome activation.

Chandan Sekhon (II BBS) – **How does spaceflight affect adult neurogenesis**

The advent of spaceflight to explore the space environment and potentially even inhabit new worlds means it is becoming increasingly crucial to understand the effects of the harsh environment beyond Earth on physiology, as this will influence healthcare, architecture, transport and life in space. It is also crucial to understand this field to inform any precautions we implement to mitigate the risks of increased radiation, altered sleep-wake cycles, microgravity, hypomagnetic field etc, on bodily function. I aim to explore this further in my dissertation as I look at how spaceflight affects the process of neurogenesis – a process inducing brain plasticity, and possible long-term effects this may have. To do this, I detail the process of neurogenesis itself, where it happens, what role it has in the brain and what regulates it. I then explore different factors that could affect the process itself, and I review appropriate literature to discuss this. The lack of experiments conducted in the space environment and the lack of studies in humans limit my ability to come to a definite conclusion. However, I hope to continue this new and emerging research with my dissertation and hopefully encourage others to do the same, thus furthering our knowledge of the field.

Will Orchard (PhD) – **Correlation implies causation**

It is often said that correlation does not imply causation. Although true, the field of causal discovery investigates in what situations and under what assumptions causal relationships can be deduced from correlations alone. In my own research, I aim to leverage causal discovery to understand how biological signalling networks change in cancers which have become resistant to drug therapy. However, as an additional challenge, we do not typically have direct measurements of protein activity and thus causal discovery must be performed using only indirect information. In this talk I give a brief introduction to causal discovery, discuss the challenge of inferring causal relationships with indirect measurements, and give some outlooks for the field.

Eleanor Sheekey (PhD) – **Confused or in control? Tales of mutant-p53 and a PhD student**

Like many PhD students I think I am studying the most important protein. The protein I study is p53, also known as the guardian of the genome. The gene encoding this protein is the most commonly mutated gene in human cancer. Most of these mutations occur in the DNA binding domain of p53 preventing the canonical function of responding to cell stress. But the story doesn't end there. These past 3.5 years I've examined what happens to cells that possess both wild-type and mutant p53 ($p53^{+/R175H}$) – an early stage of tumorigenesis – how it affects the cell fitness and how it perturbs or awakens novel DNA binding sites. Ultimately, it has led me to question, is this mutant protein simply confused, or in control?