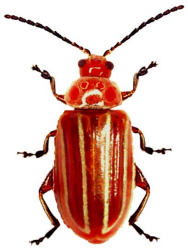

# Peterhouse Biology Symposium 2024

Saturday 24th February 2024, Peterhouse Theatre

Fani Memi (Research Associate) – **Mapping the brain tumour microenvironments using spatial transcriptomics**

Clara Dunbavin (II BBS) – **Does folic acid over-supplementation during pregnancy affect fetal development?**
Prenatal care is a pivotal factor for ensuring the health and well-being of developing fetuses and expectant mothers; this prenatal care involves a combination of early and regular check-ups, screening, nutritional guidance, and supplementation, hoping to optimise pregnancy conditions. Over the past decade there have been over 3000 publications annually on PubMed reflecting the growing focus on prenatal care.
In the 1980s the importance of folic acid (FA) in embryonic neural development was discovered, triggering a surge in research exploring broader implications of FA on neurodevelopment. The evidence pointed to FA's integral role in prevention of neural tube defects and further studies have suggested a positive impact of continued FA supplementation on mental functions such as cognition. However, with increased awareness, national fortification programs and growing availability concerns have arisen regarding over-supplementation and potential negative consequences for both mother and fetus.
The folate-methionine pathway is fundamental for gene expression: neural cell studies have revealed changes in gene expression for ion channel, neurotransmitter, and receptor proteins. There is significant variation between sexes but altered expression of certain genes have been linked to increased anxiety symptoms and highlighted links to neurodevelopmental disorders such as autism spectrum disorder. A range of studies looking at molecular, morphological, and behavioural changes in different models following FA over-supplementation show the potential role of FA in ASD aetiology. The dissertation aims to investigate the impact of FA over-supplementation on fetal development particularly concentrating on neurodevelopmental disorders and seeks to identify potential risks of excessive FA intake, offering insights for refining prenatal supplementation: an individualised approach which considers genetic factors and current intake of FA may help improve neurological outcomes and prevent neural tube defects during crucial stages of fetal development.

Graham Christie (Fellow) – **Rude awakenings: bacterial spores and how they germinate**
To the uninitiated bacterial spores may seem dull: lifeless cells just biding their time doing…. nothing. It's remarkable then that the process by which they germinate and return to life has captivated and puzzled scientists for the best part of a century. In contrast to the sloth-like incremental progress made over the bulk of that period, the past two years have been marked by a series of astonishing insights to how all of the pieces fit together. A whistlestop tour of why we should care about bacterial spores, and how they monitor and respond to environmental cues, forms the basis of this presentation.

Konstanze Schichl (PhD) – **Identifying changes in viral gene expression and biomarkers in the context of HPV-associated pathology**
The deregulation of the expression of the human papillomavirus (HPV) oncogenes E6 and E7 is the main contributor to the development of cervical cancer. Thus, it is important to identify the sites that are most vulnerable to the deregulation, as well as its possible mechanisms.
Firstly, we showed that viral RNA can be used as an indicator for the disease stage, as it only reaches the upper epithelial layers in high-grade squamous intraepithelial lesions (HSIL), while being confined to basal and mid

epithelial layers in low-grade squamous intraepithelial lesion (LSIL). Then, we identified the different biomarker and E6/E7 expression patterns in LSILs and found that not all low-grade lesions are productive viral infections, agreeing with results from previous studies stating that only 40% of LSILs harbour L1 or E4 expression. Additionally, we identified the different biomarker and gene expression patterns in HSILs, found to consistently express p16, MCM, and E6/E7 at full epithelial thickness. Moreover, HSILs seem more common at cervical crypt entrances, explaining why the TZ is a hot spot for neoplasia, possibly relating to the presence of the reserve cell niche. Finally, we showed that some HPV types might have a specific tropism for the reserve cell, as abortive HPV16 infection seems to mostly occur at the crypt entrances. Studying viral protein expression patterns will allow the understanding of mechanisms of deregulation of viral gene expression. Establishing a rationale in biomarker selection will be beneficial for HPV diagnostics and a quantitative analysis of basal RNA levels will allow to definition of a threshold for p16 expression.

Emily Naden (III Biochemistry) – **Unlocking hidden potential: Inhibitors turned activators in drug discovery**

Justin Gerlach (Fellow) – **Are we nearly there yet? The burden of proof in saving species from extinction**
When species are so threatened that extinction in the wild become inevitable conservation breeding becomes the last chance to avoid complete extinction. This can be successful and in a very small number of cases reintroduction back into the original range may be possible. Reintroduction of French Polynesian *Partula* tree snails was first attempted in 1995. Since 2015 there has been a major programme of releases. I describe the efforts taken to date and the most recent developments. The major challenge has been determining whether these releases are succeeding or not. There have been some failures, but the question remains: how do we identify success?

Danai Kontou (PhD) – **Tales from the deep: timeline of a predator invasion & its impact in freshwater lakes**
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.

Hayoung Choi (II Genetics) – **Studying twists and turns of chromatin *in silico* – nucleosomes and reversomes**

Catherine Whittle (PhD) – **Making decisions on the fly: integration of innate and learned information in *Drosophila* neural circuits**
Animals must continuously adapt their behaviour based on internal states and external environmental cues. This decision-making involves integrating innate stimulus-response pathways with learned experiences, which are processed via broadly separate circuits. In *Drosophila*, previous research has highlighted convergence neurons, which take input from neurons of the lateral horn and mushroom body, as integral circuit components in the merging of innate and learned information. However, experimental investigations into these neurons have been limited to a small number of examples involving simple approach or avoid decisions, and it is not clear how convergence circuitry operates to facilitate decision-making across the full diversity of input stimuli and contexts experienced by the fly.
To address this, I will explore an example of a novel convergence circuit linked to male pheromone detection. This circuit, identified in preliminary studies, will be investigated using experimental techniques including multiphoton calcium imaging, optogenetics and quantitative behavioural analysis. Overall, the project will elucidate the architecture and function of convergence circuits in *Drosophila*, providing insight into the neural basis of complex decision-making.

Alia dos Santos (Research Associate) – **Frozen in time: a sperm's tale**
From William Bragg's atomic structures of salt crystals and John Kendrew's first 3D protein structure using X-ray crystallography, to the more recent 'resolution-revolution' of cryo-electron microscopy (cryo-EM), structural biology has transformed our understanding of the molecular world. However, as these established techniques

become widely used and can provide atomic resolution of proteins, questions arise regarding the future of structural biology.

Until recently, structural studies were limited to reductionist approaches, whereby proteins are purified and isolated from all other components of their environment prior to their study. However, in biological systems, protein function rarely arises as a result of isolated events, but, instead, from the concerted action of several interacting proteins, lipids, intracellular forces, and small molecules. Thus, there is a growing need to develop methods that allow us to unveil the structure of proteins *in situ* – within their cellular, native, and unperturbed environment.

Here, I will show how cryo-electron tomography (cryo-ET) is arising as a powerful method for *in situ* structural biology, as I discuss my research with human sperm cells.

As spermatogenesis occurs in the testis, stem cells undergo key morphological changes: proteins in the cell reorganise; DNA hyper-condenses and specific isoforms are expressed to allow sperm maturation and successful fertilisation. In somatic cells, nuclear pore complexes regulate material transfer between the cytoplasm and the nucleus and are ubiquitously expressed at the interface between these two environments – the nuclear envelope. However, in mature sperm, nuclear pores drastically localise exclusively to the rear of the nucleus. When, how or why this happens is not clear. Similarly, how this change affects the function and structure of these proteins remains unexplored. Using cryo-ET and optical microscopy, we reveal that nuclear pores reorganise during the second step of meiosis in human testicular tissue, and we show that this is accompanied by major functional and structural changes. In the mature sperm, two of the three characteristic nuclear pore transmembrane rings are absent, locking the structure into a highly constricted conformation that is accompanied by loss of active transport.

Altogether, this works exemplifies the importance of studying biological macromolecules within their native environment, and the application of *in situ* studies as an exciting new field.