South Coast Biosciences Doctoral Training Partnership
SoCoBio DTP

2025 Annual Conference at the University of Southampton
23-25 April 2025

BOOK OF ABSTRACTS

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Biotechnology and Biological Sciences Research Council

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Guest Speaker Bios and Abstracts

Dr Richard Henderson, CH FMedSci FRS

MRC Laboratory of Molecular Biology – University of Cambridge

Richard Henderson (b. 1945) is a structural biologist with an undergraduate degree in physics from Edinburgh University (1966). He worked on the structure and mechanism of chymotrypsin for his Ph.D. with David Blow at the MRC Laboratory of Molecular Biology (LMB). As a postdoc at Yale, he developed an interest in membrane proteins and worked on voltage-gated sodium channels. With Nigel Unwin back at LMB, he used electron microscopy to determine the structure of bacteriorhodopsin in two-dimensional crystals, first at low resolution and later at atomic resolution. Most recently he has focused on single particle electron cryomicroscopy (cryoEM) in which electron images of a thin film containing the macromolecules of interest are obtained without the need for crystals, using the plunge-freeze method developed by Jacques Dubochet's group at EMBL. He shared the 2017 Chemistry Nobel prize with Dubochet and Joachim Frank.

Presentation Title: Accomplishments and potential of cryoEM in structural biology

Abstract: In the last decade, single particle electron cryomicroscopy (cryoEM) has experienced an enormous leap in its capability, due to improved electron microscopes, better detectors and better software, and this has revolutionised structural biology. I will show some topical examples and discuss potential for further improvements. I will also talk about our efforts to encourage development of less expensive cryoEM equipment such as described in McMullan et al, PNAS 120, e2312905120 - https://doi.org/10.1073/pnas.2312905120.

Prof Lindy Holden-Dye

Professor of Neurosciences, School of Biological Sciences - University of Southampton

Professor Lindy Holden-Dye (PhD, BSc, MSc, PhD, FRSB, FBPhS) holds a personal Chair in Neuroscience within Biological Sciences at the University of Southampton, UK. Her interests focus on fundamental processes of neuronal communication and she has established research expertise in invertebrate preparations to explore these processes. Through this interest she has published more than 200 research outputs and contributed to research relevant to a number of important areas of neuroscience that inform understanding of neural communication relevant to mental health. Her expertise in invertebrate neuroscience, and in particular nematode neural systems and the model genetic organism *Caenorhabditis elegans* positioned her well to participate in drug discovery and mode of action programmes for novel antiparasitics. For the last two decades she has collaborated with industry to improve prospects for parasitic nematode control. Her research group identified the molecular target for the resistance breaking anthelmintic emodepside showing it acts through a calcium-activated K+ channel SLO-1 to bring about neuromuscular paralysis in nematode worms. This discovery has paved the way for the pursuit of new approaches to the treatment of human filarial disease. The experimental approaches deployed in her research group encompass genetics through to whole animal physiology and incorporate novel methods for tracking animal behaviour and signal processing. She is also passionate about sharing her enthusiasm for neurobiology with the next generation of scientists and has supervised more than 35 postgraduate research students to completion.

Presentation Title: Learning from worms

Abstract: During my scientific career I have worked my way down the evolutionary tree, from mammals, via molluscs to nematode worms. Throughout this 30 plus years, I have collaborated extensively with industry, in particular the animal health sector. In my talk I will elaborate on how I found my scientific path and what I have learned from working with the worms. I will share the highs and lows of these experiences and endeavour to use these personal reflections to highlight some issues to consider for career progression.

Student Abstracts (in presentation order by cohort group)

3 Minute Thesis – Year 2

Presentation session 1

3MT: How to build a chloroplast: Unravelling chloroplast communication with the nucleus.

Adam Green, University of Southampton, Prof Matthew Terry, University of Southampton, Prof Martin Warren, University of Kent.

The chloroplast is the site of photosynthesis, which provides the plant with the biochemical energy used for growth and development. Chloroplasts therefore need to develop efficiently to ensure optimal photosynthetic performance. The chloroplast is an endosymbiotic organelle and thus, retains its own genetic material. However, the majority of the proteins in the chloroplast are now nuclear-encoded and post-translationally imported into the developing chloroplast. To ensure the chloroplast has everything it needs to become photosynthetically capable, it must communicate its developmental status to the nucleus in a process termed biogenic retrograde signalling. The current hypothesis is that the tetrapyrrole heme, which is synthesized in the chloroplast, is required for this signal and may itself be the signal. This project aims to test this hypothesis and examine the role of the retrograde signalling protein GUN1, which has unknown function but has recently been shown to interact with the tetrapyrrole pathway. To do this, transgenic Arabidopsis thaliana lines expressing the heme-degrading enzyme heme oxygenase in different cellular compartments are being used to determine if retrograde signalling is altered. The project will also investigate how GUN1 interacts with the tetrapyrrole biosynthesis pathway and how it regulates retrograde signalling during chloroplast biogenesis.

3MT: De Novo Design of Metallocorrin Enzymes

Alex Cahill, University of Portsmouth, Dr Bruce Lichtenstein, University of Portsmouth, Prof Martin Warren, University of Kent, Prof Ross Anderson, University of Bristol.

Vitamin B12 is an essential natural cobalamin cofactor able to catalyse chemical transformations that have proven challenging in chemistry and industry, such as dehalogenation and selective isomerisation, and is vital for DNA methylation within the body. The role vitamin B12 and its derivatives play in these processes is well established, however how proteins control its chemistry is still not well understood. De novo designed cobalamin binding proteins will allow close study of the fundamental engineering principles underlying the complex enzymes using cobalamin that are found in nature. This research aims to use recently developed deep learning tools, such as RFdiffusion all-atom and LigandMPNN, to design proteins capable of binding and utilising cobalamin, simplifying the study of the fundamentals of B12 chemistry without the complexities found within biological systems. The effectiveness of the design tools was evaluated, and the protein designs were validated using the molprobity tool. Small scale expression trials of the designs were conducted prior to large scale production, after which their binding affinities as well as

their chemical activities will be characterised in order to tease out the engineering rules for controlling B12 chemistry.

3MT: Using a holistic and multidisciplinary approach to investigate the effects of regenerative agriculture on the soil microbiome – Effect of Biochar combined with manure.

Christian Hollingbery, University of Kent, Dr Marc Dumont, University of Southampton, and Dr Anastasios Tsaousis, University of Kent.

The microbiome plays a large role in nutrient cycling, structuring, and control of physiochemical properties in the soil. Therefore, when developing sustainable or regenerative farming practices, it is key to understand their affect on the soil microbiome, and how this relates to soil properties and plant growth. The use of biochar as an amendment is one such method being explored to improve soil fertility. Biochar has a large surface area due to its network of pores, which contributes to its high sorption capacity. Thus, pre-incubation with biochar could reduce leaching from nutrient rich organic fertilisers, perhaps prolonging their effect on the microbiome. To test this biochar was incubated with various ratios of cattle and insect manure (frass) and investigated for changes to the bacteriome of soil on a plot-scale. Inclusion rates of biochar in the two manure types ranged from 0%, 10%, 25%, and 50%, which were applied to soil and bacteriome and physiochemical properties at time-points over a one-year period. After six months the greatest shifts in bacteriome, when compared to the soil only control, arise from biochar/manure combination treatments rather than the manure only, which could be indicative of a slow release of nutrients into soil.

3MT: Capture and degradation of micro-plastics by a synthetic biology approach to engineer novel PET-degrading enzyme linked amyloid nano-material

Claudia Chitty, University of Kent, Prof Louise C Serpell, University of Sussex, Prof Tobias von der Haar, University of Kent, Dr Wei-Feng Xue – University of Kent

Awaiting submission of abstract.

3MT: Manipulating the molecular features of long non-coding RNAs to regulate gene expression in an industrial context

Courteney Pienaar, University of Sussex, Prof Sarah Newbury, University of Sussex, Dr Tobias Von derHaar, University of Kent, Dr Ben Towler, University of Sussex.

Controlling RNA stability is essential for gene expression regulation and cellular homeostasis. While mRNA stability mechanisms are well-characterised, revealing links between translation and degradation, long noncoding RNA (lncRNA) stability regulation remains largely unexplored. Recent evidence indicates lncRNAs undergo translation introducing additional regulatory complexity. We hypothesise that although lncRNAs may

utilise translation-dependent decay pathways similar to mRNAs, fundamental differences likely exist in their regulation, potentially representing evolutionarily distinct control mechanisms.We investigate the relationship between lncRNA stability and translation through complementary approaches. Using ribosome profiling in HEK293T cells with targeted knockouts of exoribonucleases DIS3L2 and XRN1, we assess how these nucleases differentially impact lncRNA versus mRNA stability and translation. Concurrently, tRNA-seq in Drosophila melanogaster wing imaginal discs enables modelling of ribosome dynamics on lncRNAs, with subsequent assays evaluating stability impacts. By integrating our data with publicly available datasets, we perform cross-species comparisons to determine whether lncRNA regulatory mechanisms are conserved evolutionarily. This approach addresses a significant knowledge gap in RNA biology and provides insights into lncRNAs as post-transcriptional gene regulators in both normal physiology and disease contexts.

Presentation Session 2

3MT: Chemical Tools to Interrogate Protein-Misfolding Diseases

Daniel Aspiazu, University of Southampton, Dr Sam Thompson, University of Southampton, Dr Wei-Feng Xue, University of Kent.

Protein-protein interactions (PPIs) are physical contacts between protein domains where there is selective recognition between the proteins involved. PPIs include the misfolding of normally soluble peptides into toxic aggregates known as amyloids. This process is associated with numerous widespread and incurable diseases, including Parkinson's, Alzheimer's, and Type II diabetes. Due to the characteristically large and flat binding sites of PPIs, small molecules are often unable to interfere with such interactions and there is an unmet need for chemical probes and drugs able to interrogate protein misfolding. Many amyloid aggregates are rich in beta-sheet structures, which consist of packed linear beta-strand peptides. Synthetic mimics of beta strands that can selectively bind to beta-strand segments in amyloidogenic proteins could interfere with PPIs, inhibiting the beta-sheet assembly process which leads to aggregation. This work aims to design a new class of such synthetic beta-strand mimics, contributing to the development of a chemical toolkit for selective inhibition of amyloid formation. This will be valuable in understanding the underlying mechanisms of amyloid formation and may shed light on a way to treat these diseases.

3MT: Perennial crops for sustainable cities.

Emily Kate Millerchip, University of Sussex, Dr Daniel Ingram, University of Kent, Prof Dave Goulson, University of Sussex, Dr Elizabeth Nicholls, University of Sussex.

Urban agriculture is increasingly recognised as a strategy for more sustainable food production. Urban agriculture can also increase the health and wellbeing of urban residents, reduce warming and air pollution in cities and provide habitat for wildlife. Evidence suggests that small-scale urban agriculture can be as productive as conventional farming and typically

uses fewer synthetic fertilisers. However, consideration must be given to all aspects of resource use involved in urban agriculture to ensure it is truly sustainable. Perennial crops offer multiple benefits to agriculture, including reduced soil disturbance, increased carbon storage and resources for beneficial wildlife. However, limited studies have explored whether these benefits carry over to urban landscapes. Perennial growing may also have novel disadvantages in urban agriculture, related to their long-lasting and spreading nature. This project aims to investigate the costs and benefits of perennial cropping in urban agriculture with a focus on the effects on beneficial insects. Field surveys will quantify the effect local and landscape perennialisation has on the richness and abundance of species involved pollination and biological pest control in urban agriculture. Interviews of urban agricultural site managers will analyse the perceived positives and negatives of urban perennial growing from a multi-disciplinary viewpoint.

3MT: Adaptation to osmotic stress induces Cap1-dependent immune evasion in *Candida albicans*.

Emmanuel Denu, University of Kent, Davey Ieuan Llewellyn Kneafsey, University of Kent, Catrina Lloyd, University of Kent, Dr Rebecca Hall, University of Kent, and Prof Paul Skipp, University of Southampton.

Candida albicans is an opportunistic fungus and a commensal in the natural microbiota of humans, but can disseminate to organs, causing severe systemic infections in immunocompromised individuals, accounting for over 1.5 million incidence and 63.5% mortality each year for invasive candidiasis. As a result, the world health organization has classified *C. albicans* into the critical group of the fungal pathogen priority list. The kidney, which has the highest osmolarity amongst the organs of the body, is the most susceptible to systemic Candida infection. This raises concern on potential *C. albicans* adaptation to the osmotic environment, aiding them to evade innate immunity to cause severe infections. Here we show that adaptation of *C. albicans* to osmotic conditions that mimic the kidney environment, result in reduced immune recognition of the pathogen. Screening of key genes involved in adaptation to osmotic stress, identified that the observed innate immune evasion was dependent on the transcription factor Cap1. To identify the role of Cap1 in osmotic induced immune evasion, transcriptional profiling was performed, with differentially expressed genes being enriched with cell wall associated genes, many of which are expressed in a Cap1 dependent manner. Work is underway to identify the osmotic stress-induced immune evasion pathway.

3MT: Molecular and genetic mechanisms underlying the selective assembly of the plant microbiome through lignin precursors

Holly Champney, University of Southampton, Dr Tomislav Cernava, University of Southampton, Dr Xiangming Xu, NIAB at East Malling, Dr Franklin Nobrega, University of Southampton.

Our agricultural system depends heavily on pesticides and fertilisers, but these tools are

often ineffective and come with harmful side effects. In response, biological solutions, such as microbial inoculants, have gained popularity as a more suitable alternative. However, the rapid adaptation of pathogens makes long-term use of specific microbial strains for biocontrol unsustainable.

To address this challenge, a promising solution is to focus on altering the plant microbiome as a whole. By shifting the microbiome to a disease-resistant state, we can reduce the likelihood of pathogens overcoming this multifaceted form of resistance. In practice, this approach can be implemented by selectively breeding or genetically engineering crops based on specific genes, known as Microbiome/M genes, that shape the entire microbiome.

My research builds on knowledge that certain M genes affect plant exudation patterns which in turn shape the microbial community. By studying microbial responses to these exudation patterns, we can observe how different microbes (both beneficial and pathogenic) are enriched, inhibited or unaffected by these exudates. Specifically, I aim to uncover molecular mechanisms that enable microbes to respond to these changes, helping us determine whether modifying the plant microbiome could be a sustainable alternative to current biocontrol methods, or whether this system has already been hijacked by plant pathogens.

Presentation Session 3

3MT: Adaptation of cutting-edge photonic tools to understand food spoilage biology.

Joshua Fennell, NIAB, Prof Xiangming Xu, NIAB, Prof Adrian Podoleanu, University of Kent, Dr Matevz Papp-Rapar, NIAB.

In a sentence, the proposition of the project is to study latent and active infections of the fungal pathogen *Monilinia laxa* within cherries using optical coherence tomography (OCT). The way in which fungal pathogens penetrate and behave below the surfaces of fruit such as cherries is not wholly understood. This is largely down to the methods that have been applied to understand it, such as microscopy, which are destructive and therefore limit our ability to monitor samples over time. The use of OCT allows us to look at whole cherries non-destructively to a depth of 1000µm, providing a structural picture of what may be occurring with both the pathogen and plant cells. Furthermore, novel methods within OCT such as PS-OCT (Polarisation Sensitive) and Dynamic OCT will be utilised to see if they can provide better contrast between the plant cells and fungi and allow for potential quantification of the extent of infection below the fruits surface. Ultimately the project hopes to showcase the use of OCT in boosting our understanding of fungal pathogens within fruit with the aim of allowing us to develop better strategies at tackling it, thereby reducing food waste at all stages of the fruit supply stage.

3MT: Designing glial derived exosomes for nervous system repair

Joshua Byrne, University of Southampton, Dr Melissa Andrews, University of Southampton, Prof Arthur Butt, University of Portsmouth

Axon regeneration after traumatic injury is difficult to achieve within the mature spinal cord. α9 integrin, a transmembrane receptor that mediates communication between the cell and the extracellular environment, can promote the regrowth of injured axons. However, when this integrin is artificially over-expressed in mature neurones these proteins are not trafficked within the axon. This project aims to investigate exosomes, small extra-cellular vesicles that mediate cell-cell communication, as a physiological carrier of α9 integrin. As part of this project, CNS glia, specifically Olfactory Ensheathing Cells (OECs) and Astrocytes, as well as Embryonic Fibroblasts will be investigated as potential sources for α9 integrin-carrying exosomes. Secreted exosomes from a9-expressing cells will be tested for their ability to carry functioning integrin to target cells and promote neurite growth. Further, features that will enhance consistent delivery of integrins via exosomes, such as improving the yield and stability of sEV's collected, will also be investigated.

3MT: New Chemical Tools for Understanding Drug-Microbiota Interactions in Parkinson's Disease

Linda Guantai, University of Southampton, Dr Sam Thompson, University of Southampton, Ella Bavinton, University of Southampton, Prof Sumeet Mahajan, University of Southampton, Dr Fatima Pereira, University of Southampton, Institute for Life Science, University of Southampton.

The Parkinson's disease drug entacapone affects gut microbiota, altering commensal growth and selecting for species with pathogenic potential. It also accumulates in microbiota cells, but the species involved, and the molecular basis of this accumulation remain unclear. Here, we used entacapone derivatives compatible with click-chemistry and bioorthogonal labelling to visualize interacting species and study its bioaccumulation dynamics. Faecal samples from three healthy individuals were incubated ex vivo with entacapone and two alkyne-modified derivatives. Flow cytometry and 16S rRNA gene sequencing assessed microbial load and composition. Both derivatives reduced microbial load and altered community composition similarly to the native drug. Fluorescence labelling and sorting identified interacting taxa, revealing broad microbial interactions rather than species-specific accumulation. This study highlights entacapone derivatives as valuable tools for investigating drug-microbiome interactions. Given the microbiome's role in host health, these alterations may contribute to dysbiosis, altered drug metabolism, and worsening Parkinson's symptoms. Understanding these effects is crucial for optimizing therapeutic regimens, minimizing microbiome-associated health risks, and improving patient outcomes. Future studies should explore whether probiotics or dietary modifications can mitigate these disruptions, advancing safer treatment strategies for Parkinson's disease.

3MT: Understanding the genomics and ecology of floral nectar to enhance crop-pollinator interactions

Lucy Unwin, University of Sussex, Dr Maria Clara Castellanos, University of Sussex, Prof Mark Chapman, University of Southampton.

Floral nectar, as the primary reward offered by flowering plants to pollinators, plays a crucial role in maintaining plant-pollinator interactions. These interactions are vital for maintaining food security, global sustainable agriculture, and ecosystem function. Biotic pollination is known to enhance both the quality and quantity of yields for many important crops. However, the ongoing decline in pollinator populations worldwide presents a significant threat to these interactions. 'Nectar-enhanced' cultivars of crops with more desirable nectar traits, such as larger volumes or higher sugar concentration, could be developed to optimize insect visitation. This would provide benefits both to crop yields and pollinator populations. Recent research has demonstrated that nectar traits can vary widely both within and between species. However, the genetic basis, plasticity, and ecological costs of this nectar trait variation remain poorly understood. Understanding these aspects of nectar biology is critical when considering strategies to develop crop varieties that balance the benefits of enhanced pollinator attraction with the plant's overall fitness and productivity. My PhD project aims to explore these ecological and genetic interactions underlying nectar variation and nectar trait plasticity, assessing their roles in successful pollination and therefore the viability of selecting nectar-enhanced crop varieties.

Presentation Session 4

3MT: Investigating how SKN-1B-mediated neuronal signalling controls appetite behaviours

Lydia Bennett, University of Kent, James Evans, University of Kent, Dr Tim Fenton, University of Southampton, and Prof Michelle Garrett, University of Kent, Dr Jennifer Tullet, University of Kent.

Obesity is a growing global health crisis, often leading to metabolic disorders. Appetite influences food intake and is therefore a contributing factor. Appetite control is a good point of intervention. Both humans and C. elegans have similar appetite control mechanisms, meaning we can use worms as a simple model to understand the molecular basis of appetite. Our lab has identified SKN-1B as a regulator of appetite control in C. elegans. SKN-1B is expressed in two chemosensory neurons (ASIs) and is orthologous to mammalian Nrf transcription factors. skn-1b mutants explore bacterial lawns less than wild-type (WT) and exhibit increased satiety responses.

Understanding how neuronal SKN-1B communicates with other tissues to regulate behaviour is crucial for identifying molecular pathways controlling appetite. We hypothesised that SKN-1B utilises neurotransmitters for this function and tested mutant strains lacking neurotransmitter synthesis enzymes. tdc-1 mutants cannot synthesise tyramine. Both skn-1b and tdc-1 mutants showed reduced exploration, but double mutants had no additive effect, suggesting tyramine may be involved. Feeding skn-1b mutants Providencia, which produces tyramine, restored exploration. However, a Providencia

mutant lacking tyramine also rescued exploration, indicating a complex interaction. Thus, tyramine alone cannot explain SKN-1B-mediated behaviour, and additional pathways must be involved.

3MT: Group-living spiders as biological control agents

Thomas Roberts-McEwen, Dr Lena Grinsted, and Prof Matt Guille, University of Portsmouth
Prof Alan Stuart, University of Sussex, Dr Yann Bourgeois, Institute de Recherche Pour le Développement.

The introduction of invasive agricultural pests forces reliance on toxic chemical insecticides, giving rise to pesticide resistance in insects that significantly damage crop yields. It is therefore important to assess the efficacy of natural predators as biological pest control agents.

Spiders are among the most abundant generalist predators, contributing to pest control in agroecosystems globally. However, most species are solitary and highly cannibalistic, reducing their biocontrol efficacy. In contrast, our communal focal species (*Cyrtophora citricola*) is highly tolerant of neighbours, creating remarkable predator-dense colonies. This trait could make them uniquely suited to a role in biocontrol- an avenue of research yet to be explored.

Prior to their encouragement into agroecosystems, it is important to understand the impact that communal spiders may have on both pests and agriculturally beneficial invertebrates such as pollinators. Using metabarcoding, we will ascertain the diet composition of group-living spiders, enabling the exploration of trophic interactions within agroecosystems. Bioinformatics will reveal which pest species are being caught, and whether beneficial insect populations are being detrimentally affected. This research will therefore provide insight that will allow us to accurately assess the suitability of communal spiders as biological control agents of agricultural insect pests.

3MT: Exploiting natural variants in potassium channel genes to understand their roles in neural function, behaviour and development.

Tia Fletcher, University of Portsmouth, Dr Annie Godwin, University of Portsmouth, Prof Matthew Guille, University of Portsmouth, Dr Mariana Vargas-Caballero, University of Southampton, Prof Diana Baralle, University of Southampton.

The Global Genes Project estimates 350 million people have a rare disease, ~80% of which are genetic. Diagnosis of novel rare diseases is challenging with around half of current patients undiagnosed. Molecular diagnoses enable specialised treatment and substantially improve patient outcomes; only 30% of undiagnosed patients with a rare disorders reach their 5th birthday, rising to 70% after diagnosis. Genetic channelopathies are rare disorders caused by variants in genes that code for ion channels, leading to disruptions in electrical signals and potentially causing various neurological and cardiac problems. Diagnoses rely on

functional evidence to link genotype and phenotype. Rare disorders have limited patient populations, so functional evidence from patient data is diagnostically insufficient. Animal models, like Xenopus frogs, thus remain indispensable to test gene variant-disease links, providing diagnoses. Xenopus frogs have been shown to be powerful models of rare genetic diseases; they have more than 80% of known human disease genes, a beautifully annotated diploid genome sharing its structure with humans and produce hundreds of embryos that can be genome engineered in a few hours, even targeting specific organs.

Presentation Session 5

3MT: Using AI and big data to identify a set of biologically validated drug targets for hard-to-treat cancers

Daniel Beach, University of Sussex, Prof Stuart Farrow, Cancer Research Horizons, Prof Michelle Garrett, University of Kent, Dr Frances Pearl, University of Sussex

Cancer remains a major global health challenge, with 19.3 million new cases and 10 million deaths reported in 2020. While survival rates have improved over recent decades, some cancers remain extremely difficult to treat. These include pancreatic, brain, liver, stomach, and oesophageal cancers, where fewer than 1 in 10 people survive five years after diagnosis. For these cancers, there has been little progress in survival since the 1970s, and there are few new treatments in development. Cancer cells often rely on genes that are expendable in healthy cells. These “cancer-essential” genes are promising drug targets because blocking them can kill cancer cells without harming healthy tissue. CRISPR screening studies have mapped these gene dependencies in cancer cell lines but identifying them in individual patients is impractical at scale using current methods. We also still need to understand what makes a cancer dependent on a particular gene - such as co-existing mutations or expression changes - how common these dependencies are in the patient population, and whether they are druggable. Working with Cancer Research Horizons and the University of Kent, my research focuses on developing AI models and computational tools to find and validate new drug targets for hard-to-treat cancers. By analysing multi-omics genetic data and building better predictive models of gene dependency, I aim to identify the most promising targets for future precision therapies.

3MT: Dry biofilms: what's going on...ON the surface?

Macy M. Martin, University of Southampton, Mr Mike McGrath, Copper Cover Ltd (UK branch of Necon Technologies), Prof C. William Keevil, University of Southampton, Dr Sandra A. Wilks, University of Southampton.

Healthcare-associated infections (HAIs) are a global burden with high mortality rates, often from multidrug-resistant bacteria. Many cases arise from patient contact with contaminated hospital surfaces, exacerbated by patients’ immunocompromised states. As studies show bacterial contamination can persist on hospital surfaces despite rigorous cleaning procedures, one explanation for bacterial survival may be the presence of dry surface

biofilms (DSBs).

A recent identification in the biofilm field, DSBs form and survive long-term in the presence of extremely little moisture and are often resistant to chemical and physical removal. DSB discovery may provide insight to how biofilms can tolerate long-term osmotic stress and perpetuate HAIs; however, with few DSB studies available in the literature, many details of their structure, development and removal remain elusive. This research aims to model DSB formation on high-contact surfaces over time using controlled laboratory methods, with quantitative culture methods and fluorescent microscopy used to understand cell and matrix properties.

Public infection prevention strategies must be strengthened to overcome antimicrobial resistance as antibiotic breakthroughs falter. Copper is a known antimicrobial material, and in partnership with Copper Cover this research will investigate the ability of copper alloys to combat laboratory-grown DSBs, and evaluate long-term impacts of copper surfaces on environmental microbiomes.

3MT: Understanding adult stem cell-niche interactions using the Drosophila intestine

Miya Giragosian, University of Kent, Dr Jerome Korzelius, University of Kent, Dr Nahuel Villegas, Vivan Therapeutics.

The human intestine is maintained by intestinal stem cells (ISCs) which differentiate into two main types of cells: absorptive enterocytes (ECs) and secretory enteroendocrine cells (EEs). Dysregulation of ISC proliferation is caused by ageing, diet, and genetic factors which can lead to inflammation and tumorigenesis. However, identifying signals from the surrounding epithelium that influence ISCs remains an underexplored aspect of intestinal stem cell biology.

Drosophila melanogaster provides an anatomically and genetically similar model to humans for studying conserved regulatory processes in healthy and diseased intestines. We are developing an inducible system to simultaneously stimulate ISC overgrowth in the intestinal epithelium and manipulate expression of secreted molecules from surrounding differentiated cells. Combining two different bipartite inducible transcription systems allows us to identify which key factors released by differentiated cells affect the ISC niche environment. We will also assess survival in flies with downregulated candidate genes to identify molecules that enhance or suppress ISC proliferation, differentiation, and impact overall lifespan. Finally, we will test conserved gene hits from Drosophila work in human intestinal organoid cultures to identify novel conserved factors in ISC maintenance and proliferation. This work will aid in a better understanding of gut tissue maintenance mechanisms across species.

3MT: Development of novel methods for RNA phage discovery.

Rachel Buchanan, University of Southampton, Dr Nela Nikolic, University of Southampton, , Dr Matthew Wand, Dr Franklin L. Nobrega, University of Southampton, Institute for Life Science, University of Southampton

Traditional phage isolation methods have led to a bias towards dsDNA phages, with RNA phages and their role in microbial communities left largely unknown. Along with the need to overcome bacterial defence systems, RNA phages rely on receptors not found in common lab strains. Thus, the true diversity of RNA phages shown in metagenomic studies has yet to translate to lab-based isolation methodology. Here, we propose new methods combining differential fluorescence and density gradients to distinguish DNA and RNA phages on concentrated virome samples, along with the production of bacterial strains deficient of known defence systems. We anticipate our methods will expand upon the known diversity of isolated phages and allow the development of DNA and RNA phage panels for future research against multidrug-resistant bacteria.

3MT: Imaging ATP Usage in Cardiac Muscle to Investigate Contractile Dysfunction

Ateeqa Naim, University of Kent, Matvey Pilagov, University of Kent, Dr Sonette Steczina, University of Washington, Prof Michael Regnier, University of Washington, Prof Michael A. Geeves, University of Kent, Jeremy Graham, Cairns Research, and Prof Neil M. Kad, University of Kent.

Cardiac muscle contraction results from interactions between the force-generating motor protein myosin, and the actin-containing thin filament within the sarcomere, the fundamental contractile unit. Myosin generate force through ATP hydrolysis, therefore, given the vast number of myosins in the heart, if all were producing force simultaneously this would lead to hypercontractility, delayed relaxation and a detrimentally rapid depletion of ATP. To prevent this, a slow ATPase state, termed the ‘super relaxed’ (SRX) state exists in which a population of myosins reside until they are recruited, typically during increased stress (e.g., during exercise). However, in diseases such as hypertrophic cardiomyopathy (HCM), the most common genetic heart disease, affecting 1 in 500 people, it is suggested that the population of myosin in this cardioprotective SRX state is significantly reduced. Our research aims to utilise single-molecule imaging to determine the spatial distribution of this SRX myosin population across the sarcomere and understand how this distribution is dysregulated by disease-associated mutations, force and pharmacological interventions. Ultimately, we aim to scrutinise the cardiac contractile system at a single molecule level to develop a comprehensive understanding of cardiac myosin regulation.

Presentation Session 6

3MT: Investigating Manipulation and Engineering of the Lipid Metabolic Pathway in CHO Cells to Improve the Downstream Processing of Cell Culture Supernatants

Thomas Jamieson, University of Kent, Dr Mark Ellis, UCB, Matthew Hinchliffe, UCB, James White, UCB, Prof Mark Smales, University of Kent.

Chinese hamster ovary (CHO) cells are the current industrial system of choice for the expression of complex, post-translationally modified recombinant biopharmaceutical proteins. For many monoclonal antibodies (mAbs) production yields of 5g/L and higher are routinely achieved, however many new format and antibody inspired modalities (such as Bispecific antibodies) can be difficult to express and/or cellular components can present problematic downstream processing issues. Recent research has shown that upregulation of key genes responsible for lipid metabolism in CHO cells can result in an expansion of the ER, leading to increased secretory biotherapeutic recombinant protein production. This project will investigate (1) bioprocesses that modulate lipid metabolism in a cell line specific manner, which ultimately impact downstream processing, and (2) manipulation of key genes and pathways in lipid metabolism in CHO DG44 and CHOK1 host cell lines, determining the subsequent impact on culture viability, cell growth, yield and quality of secreted biotherapeutic protein, vesicle (specifically exosome) production and on primary downstream processing events.

3MT: Characterisation of the molecular and physiological effects of SENTIA® in the mammalian enteric nervous system.

Ana Carolina Ferreira, University of Portsmouth, Delia Belelli, GABA Labs, David Nutt, GABA Labs, Dr Murphy Wan, University of Portsmouth, Dr Jerome D Swinny, University of Portsmouth.

SENTIA is a beverage composed of a number of plant-based extracts, developed to mimic the positive effects of alcohol, specifically increased sociability. A potential target could be the enteric nervous system (ENS), whereby Sentia may modulate the brain-gut axis, an important contributor to brain functions and behaviours.

However, the effects of SENTIA on the ENS have yet to be explored. Thus, the aims of my project are to determine the effect of SENTIA on intrinsic gut function, and the underlying biological mechanisms.

In this initial part of my PhD, I used isolated segments of the mouse intestine, in an organ bath preparation, to determine the effects of applied SENTIA on spontaneous intestinal contractility. I then used RNAseq to explore potential biological pathways engaged by SENTIA in the gut.
SENTIA overall induced relaxation of both the ileum and colon, by decreasing the basal tone, the frequency and amplitude of contractions.

Transcriptomics analysis revealed that SENTIA altered the expression of genes associated with a myriad of biological pathways, in a sex and gut region-dependent manner. Overall, SENTIA induces a gut physiological phenotype reminiscent of behavioural relaxation.

Next, I will compare SENTIA with alcohol, and explore their pharmacological profiles in the gut.

3MT: To stop the proton wave in the intestine – a chemical route for mitigation of parasitic nematodes utilising Vacuolar Proton Pump-ATPase

Liliana Jeziorska-Clifford, University of Southampton, 2025Project Group, University of Southampton, James Dillon, University of Southampton, Marcus Guest, Syngenta, Prof Vincent O'Connor, University of Southampton.

Chemical treatments are important routes to the mitigation of plant-parasitic nematodes, however these control strategies are often bound to a lack of selectivity, leading to off-target effects. Thus, it is crucial to develop specific and selective anti-parasitic strategies, which could include the use of nanobodies. Nanobodies are small immunoglobulins derived from camelid heavy-chain-only antibodies, which are characterised by higher target selectivity compared to conventional antibodies. Given the long and complex parasitic life cycle, we can use Caenorhabditis elegans as a model organism to test novel mitigation strategies for parasitic nematodes. Ideally, any proposed target tissue should be readily accessible by the drug and essential for survival, such as the intestine, pharynx and sensory neurons. To extract targets essential for the nematode's survival, a bioinformatic pipeline was designed to find proteins with exposed loops to the luminal side of the intestine. vha-6, which encodes the a3 subunit of the Vacuolar Proton Pump-ATPase, was prioritised as a top candidate as it is essential for development and nutrient uptake. We further recombined it using CRISPR/Cas-9 engineering to co-express the recombined ALFA-tag epitope to test its capacity to bind to externally delivered nanobodies using anti-ALFA-tag nanobodies.

3MT: Metal analogues of Vitamin B12

Emily Jones, University of Southampton, Prof Martin Warren, University of Kent, Dr Andrew Lawrence, University of Southampton.

Vitamin B12 is an essential vitamin to sustain life, being a cofactor for two enzymes in the body, methionine synthase and methyl-malonyl CoA mutase which are responsible for essential metabolic processes. Metal analogues of B12 can be antivitamins, meaning that they have a similar structure to B12 but lack its metabolic activity. Due to the reliance on this vitamin for life, there are several theoretical uses for these metal analogues, such as antimicrobial and anti-cancer agents as they could 'block up' essential metabolic pathways required for the proliferation of bacteria and cancer cells. This work focuses on the synthesis of a range of metal analogues of B12, and exploring these potential applications. Synthesis of these compounds consists of using genetically modified E. coli to produce a metal free

metabolic intermediate of B12, hydrogenobyric acid, which is a corrin ring, before inserting metals chemically in the place of cobalt. These compounds can then be used in anticancer and antimicrobial assays.

Poster Sessions – Year 3

Poster session 1

Poster #1: Deciphering the bacterial signalling: Aptablotting of the HptRS two-component system in Staphylococcus aureus

Abhishek Johan Issac, University of Southampton, Dr Christopher Mulligan, University of Kent, Dr Seung Lee, University of Southampton.

Bacteria use two-component systems (TCSs) as a means of signalling and regulation of responses to a variety of environmental stimuli. The TCSs are made up of a sensor histidine kinase (HK) and response regulator (RR). The project aims to study the Hpt TCS and the Sae TCS from Staphylococcus aureus. The plan is to first generate small single-stranded DNA, called aptamers, that can complementarily bind to key regions of the HK and RR of each TCS. The aptamers will be subsequently tested to quantify their binding affinity with the target regions of the TCS proteins. The best target-binding aptamers will then be used for in vivo testing, using S. aureus wild-type and mutated TCS strains. The cells would be lysed and subsequently exposed to the previously selected high-affinity aptamers, to comparatively test aptamer binding with their target proteins from a former cell environment, between the wild-type and mutants. This binding affinity testing will be done using a modified Western blot, with aptamers instead of antibodies. This modified Western blot is termed an aptablot, and aims to increase the versatility of binding affinity testing for proteins by using aptamers over antibodies.

Poster #2: Risky decision-making: Revealing the neural mechanisms of behaviour selection that maximise survival.

Annie Robertson, University of Sussex, Prof George Kemenes, University of Sussex, Dr Arjuna Ratnayaka, University of Southampton, Prof Kevin Staras, University of Sussex.

To maximise survival, animals must combine sensory inputs from their environment with information about their internal state (e.g. hunger state) to select appropriate actions. However, the nature of these inputs can lead to conflicts in decision-making: for example, does a hungry animal under immediate threat of predation choose to feed or escape? Despite its importance, the neural mechanisms involved remain poorly understood. Here we exploit the rich behaviours and accessible neural circuitry of the mollusc, *Lymnaea stagnalis*, a classic neuroscientific model, to investigate action selection and the underlying decision-making mechanisms. Using a newly developed paradigm, we demonstrate that fed animals exposed to predator cues engage in anti-predator responses (escape/withdrawal), while hungry animals reverse these actions to maximise food-searching at the increased risk of predation. To explore the neural basis of this reconfiguration, we have established a novel ex vivo imaging technique, based on voltage-sensitive dyes, to assay activity in hundreds of neurons simultaneously. This is revealing key neural targets involved in the perception and evaluation of threat cues across the central nervous system. Collectively, the work

presented here provides unique insight into the adaptive mechanisms driving decision-making when animals are faced with motivational conflicts for survival.

Poster #3: Targeting potassium channels in oligodendrocytes to maintain myelin and a healthy brain across the lifespan

Ian Hunter, University of Portsmouth, Dr Anthony Lewis, University of Portsmouth, Dr Emma Veale, University of Kent, and Arthur M. Butt, University of Portsmouth.

The inward rectifying potassium channel Kir7.1 has emerged as a key regulator of cellular homeostasis in the central nervous system, yet its role in long-term neural integrity remains poorly defined. Given the critical function of ion channels in maintaining neuronal function, further investigation into Kir7.1-mediated mechanisms is essential. Potassium channel dysfunction has been implicated in age-related neurodegenerative processes, highlighting the need to elucidate their contributions to cellular stability. We are currently focused on age-comparative immunolabeling studies in the mouse brain to examine Kir7.1 expression dynamics across the lifespan. In parallel, calcium imaging experiments utilizing the Kir7.1 specific antagonist ML 418 have been performed to assess its broader functional significance in cellular activity. These investigations aim to define how Kir7.1 regulation influences neural homeostasis and may provide critical insight into its role in sustaining central nervous system function over time. Understanding these mechanisms will be instrumental in determining whether Kir7.1 modulation represents a viable target for preserving neural integrity during aging.

Poster #4: Developing novel techniques to elucidate the uptake and permeability of compounds across biological membranes

Matthew Rice, University of Kent, Prof Jennifer R. Hiscock, University of Kent, Dr Neil Wells, University of Southampton, and Dr Charlotte Hind, UK Health and Security Agency, Dr Jose L. Ortega-Roldan, University of Kent.

Biological membranes present a significant barrier to the development of new antibiotics, antifungal agents, and anticancer treatments. Understanding the permeability of clinically relevant compounds across diverse membrane types is crucial for optimising drug design, delivery, and efficacy. The lipid composition of these membranes varies significantly across species and can also change within the same cancer type or organism upon the development of drug resistance, contributing to antimicrobial resistance and reduced treatment effectiveness. These variations pose challenges for therapeutic development, requiring new strategies to assess and enhance drug permeability.
This work presents novel techniques to quantify membrane adhesion, passive permeability, and active uptake of compounds across biological membranes. The first technique enables real-time measurement of active uptake, originally developed for antimicrobial research in bacteria but now extended to nutraceutical and foliar applications. The second technique employs solution NMR to assess passive permeability and membrane adhesion properties, introducing the permeation factor (PF) and membrane adhesion factor (MAF) as

quantifiable metrics. These methodologies provide valuable insights into drug-membrane interactions, aiding drug discovery, resistance mitigation, and optimizing nutrient absorption in the nutraceutical and agricultural industries.

Poster #5: Identifying microRNA-mRNA networks involved in carboplatin resistance in lung and ovarian cancer

Nikolaos Sideris, University of Sussex, Dr Benjamin Towler, University of Sussex, Prof Martin Michaelis, University of Kent, Dr Mark Wass, University of Kent, Dr Leandro Castellano, University of Sussex.

Carboplatin is a platinum-based DNA-damaging agent used in chemotherapeutic regimens for treating lung and ovarian cancers. Despite improved survival rates, most patients eventually relapse due to resistance, though the underlying mechanisms remain unclear. MicroRNAs, small non-coding transcripts that repress gene expression on the post-transcriptional level, have emerged as key players in cancer progression and drug resistance. Evidence suggests they regulate genes crucial to resistance, but their role in carboplatin resistance has not been fully investigated. We hypothesize that miRNA-mRNA interaction networks contribute to carboplatin resistance. This project aims to interrogate these networks. Using small RNA sequencing, we identified dysregulated microRNAs and will define their mRNA targets to uncover pathways involved in resistance. At this stage, we have selected common differentially expressed microRNAs for validation and characterization. Future plans include utilizing oligonucleotide inhibitor and microRNA mimic experiments to assess how these miRNAs influence carboplatin resistance. Understanding the processes that drive resistance is key to developing effective strategies to overcome it. Therefore, identifying the networks involved will provide insights into resistance mechanisms and pave the way for new prognostic biomarkers and therapeutic approaches.

Poster #6: Viral variants: assessing the impact of natural strain variation on the structure and function of virus replication and transcription factors

Rhianne Broadway, University of Sussex, Prof Mark Wass, University of Kent, Prof Michelle West, University of Sussex.

Epstein-Barr virus (EBV) is a commonly acquired viral infection that persists within the host by immortalising the B-cells maintaining its genome as an episome. Epstein-Barr Virus is found within a range of cancers, most commonly lymphoma and nasopharyngeal carcinoma. EBV Nuclear Antigen 1 (EBNA1) is a viral protein that is crucial to the replication and maintenance of the viral genome, tethering the viral episome to host chromosomes for faithful segregation into daughter cells. Four variants of EBNA1 have previously been described based on differences in specific amino acid sequence in the C-terminal DNA binding domain (DBD) but the different varying amino acids within the N-terminal region and their function are more obscure. This project aims to examine whether the co-association of variation in the N-terminus and C-terminus of EBNA1 is functionally important

for latent EBV DNA replication and genome maintenance and determine the structural basis for this co-associated variation. We hypothesise that the N-terminus of EBNA1 and the C-terminal DNA binding domain may be in contact within the folded full length EBNA1 three-dimensional structure when bound to the latent origin of replication in the EBV genome. We have failed to demonstrate any significant difference between wild type EBNA1 and less common variants of EBNA1 on episomal DNA replication in experiment to date. However, further work will be conducted to examine the tertiary complex formation of EBNA1 N-terminus and the DNA-binding domain, perform additional DNA replication assays and elucidation of the 3D structure of the N-terminal region of EBNA1 using computational modelling and X-ray crystallography.

Poster #7: Studying the effects of reintroduction on the microbiome of the European bison

William JS Edwards, University of Kent, Yaseen Majid Salman Al-Adilee, University of Kent, Hannah Mackins, Kent Wildlife Trust, Richard Griffiths, University of Kent, Eleni Gentekaki, University of Nikosia, Dr Marc Dumont, University of Southampton, Dr Gary Robinson, University of Kent, Dr Rob Barker, University of Kent, Anastasios D. Tsaousis, University of Kent.

The wilder Blean rewilding project is an attempt to restore/improve the biodiversity of the Wilder Blean woodland (located near the university of Kent), utilising native animals or restoring extinct species, to serve as ecological engineers, notably the European bison (*Bison bonasus*).

The natural behaviour of these animals, such as wallowing, has been shown to improve flora and fauna diversity, and helping to prevent monocultures.

This study monitored the European bison, with 'bison rangers' collecting faecal samples for microbiome and parasite analysis.

To monitor the changes in the microbiome, extracted DNA was sent for Illumina next gen sequencing, using 16s primers to detect changes in the bacterial and archaeal microbiome. In the months following arrival at Blean, the bison microbiome underwent significant changes, with similar trends in microbial adjustment composition across the whole herd.

This allowed identification of 'biomarker' taxa via linear discriminant analysis and revealed negative correlation between multiple pathogenic species and the post reintroduction samples.

Poster session 2

Poster #8: Killing Intracellular Pathogens with Antibiotic Nanocapsules

Alex Clarke, University of Southampton, Adam Whelan, DSTL Porton Down, Dr Seung Lee, University of Southampton, Dr Tracey Newman, University of Southampton, Dr Mark Shepherd, University of Kent, Dr Liku Tezera, University of Southampton, Prof Nicholas Evans, University of Southampton.

Antimicrobial resistance (AMR) is an increasing problem worldwide, with a predicted 10 million deaths a year from antibiotic-resistant infections by 2050, and no new antibiotics have been approved for over 20 years. An alternative method for overcoming AMR is the repackaging of existing therapies to improve their efficacy and reduce toxicity. In particular, nanocapsules made of polymer (polymersomes) loaded with antibiotics can be used to effectively eliminate intracellular bacterial infection, without affecting uninfected cells. This work aims to see if anti-tuberculosis drugs can be successfully encapsulated in polymersomes and whether these encapsulated drugs are able to cause death of *Mycobacterium* species.

Polymersomes made of PEO-b-PCL loaded with doxycycline and rifampicin were made by nanoprecipitation and characterised. Drug-loaded polymersomes were added to free-living and intracellular *Mycobacterium smegmatis* and *Mycobacterium tuberculosis* cultures and bacterial growth and death measured. The effect of polymersomes on bacterial growth was compared to that of free antibiotic and polymer alone.

Doxycycline and rifampicin can easily and consistently be encapsulated within polymersomes. Although free drug can effectively kill *M. smegmatis* and *M. tuberculosis*, encapsulated drug does not kill free-living bacteria, but shows some effect on intracellular bacteria.

Poster #9: Raman Spectroscopy and Molecular Dynamics to Shed Light on Process of Tau Aggregation in Alzheimer's Disease

Callum Ellis, University of Southampton, Prof Sumeet Mahajan, University of Southampton, Prof Louise Serpell, University of Sussex, Prof Amrit Mudher, University of Southampton, Prof Jonathan Essex, University of Southampton.

Neurodegenerative diseases are a group of diseases manifesting in progressive cognitive decline. Despite their heterogeneity, a frequently shared hallmark is tau accumulation. However, the precise mechanisms by which tau aggregates and forms pathogenic oligomers and fibrils remains poorly defined. The pathology-associated conformational changes which lead to this accumulation are disease specific and so understanding relevance of these conformational changes could aid drug design to combat the aggregation. Tau aggregation in AD is primarily driven by association of two 6 amino acid sequences, PHF6 and PHF6* and are the focus of our work.

Using Raman spectroscopy in range of solvents, we hope to categorise the vibrational frequency shift of a vibrational probe in response to a range of dielectric conditions, thus allowing calculation of the electric field experienced by the probe. The electric field

experienced by a molecule can be thought of as the sum of all the interactions experienced on the molecule, including solvent interactions e.g. dipole interactions and gives a profile of the environment experienced by the molecule at a given time.

The calculation of electric fields can be compared to those predicted by Molecular Dynamics (MD) simulations to validate and calibrate the results of MD simulations.

Through this technique we hope to validate the results of tau aggregation in-silico MD experiments and thus potentially provide a framework to apply to other protein aggregates and a platform to test potential therapeutics.

Poster #10: Sex differences in the behavioural roles of cue-reactive orbitofrontal cortex ensembles

Emily C. Woods, University of Sussex, Kate Z. Peters, University of Sussex, Zuzana Pedan, University of Sussex, Scott B. Kinghorn, University of Sussex, Olga Tsaponina, University of Sussex, Prof Jerome Swinny, University of Portsmouth, Dr Eisuke Koya, University of Sussex.

Food cues, such as fast-food advertisements can provoke food cravings, which lead to overeating. In laboratory animals, such cues elicit food-seeking and neuronal ensemble recruitment in the orbitofrontal cortex (OFC), which modulates motivated-behaviours guided by appetitive 'cue-food' associations. Although much research has revealed sex differences in food-motivation and regional brain activity, much remains to be established regarding sex-differences in neuronal ensemble function. Here, we investigated sex-differences in OFC ensemble functioning related to cue-evoked food-seeking. To this end, we tested the effects of chemogenetic silencing of cue-reactive OFC -ensembles on sucrose-seeking in sucrose-conditioned FosTRAP2 mice. OFC ensemble silencing decreased and enhanced cue-evoked sucrose seeking in males and female mice, respectively. This silencing had no effect on sucrose-consumption in both sexes, indicating that silencing effects were cue-driven and not due to differences in sucrose reward value. Since sucrose seeking was enhanced in female mice, our silencing may have acted on inhibitory interneurons and produced this behavioural effect through disinhibition of OFC output neurons. Studies to reveal sex-differences in the composition of inhibitory interneurons are now underway. Our findings reveal that OFC-ensembles modulate food seeking in a sex-dependent manner and provide new mechanistic insights into why sex-differences exist regarding food-cue -reactivity and cravings.

Poster #11: Breaking the rule of 5: exploration of VHL-based PROTACs to increase their therapeutic viability.

Johanna A. Fish, University of Southampton, Dr Mattias G. J. Baud, University of Southampton, Prof Georgios Giamas, University of Sussex, Prof David C. Harrowven, University of Southampton, Institute for Life Science, University of Southampton

Protein-protein interactions (PPIs) play a significant role in almost all biological processes, making them a valuable commodity for disease management. Proteolysis-targeting chimeras (PROTACs) target PPIs and induce targeted protein degradation, but deviating from Lipinski's rule of 5 creates problems with their pharmaceutical properties. These are particularly pertinent with von-Hippel Lindau (VHL)-based PROTACs. Our research utilises computationally directed results combined with extensive experience in organic chemistry to produce novel molecules with improved physicochemical properties.

Firstly, we synthetically modified specific functional groups of the VHL-binding warhead to improve ligand properties, e.g., aqueous solubility. Our 'best fit' was identified by close monitoring of the binding affinity by fluorescence polarisation (FP) assays, before shifting our attention to consider the entire PROTAC construct via the linker attachment point on the VHL ligand. We envisaged novel connection points from proof-of-concept synthetic methodologies developed in Southampton. Work is ongoing to develop a robust methodology for these exit vectors, before building a library of PROTACs for further evaluation in cellular environments. We expect to further aid our understanding of the tertiary structure of these PROTACs by crystallising the lead compounds with the VCB protein, which could elucidate further on the structure-activity relationship (SAR) of the VHL-binding pocket.

Poster #12: Intracellular-targeting novel compounds and the exploitation of cell membranes and membrane transporters.

Olivia Keers, Prof Jennifer Hiscock, Prof Michelle Garrett, University of Kent, Prof Jonathan Essex, University of Southampton, Dr Hamish Ryder, CRUK Therapeutic Discovery Laboratories.

In the UK, there are around 170,000 deaths a year attributed to cancer, which in 2021 was equivalent to one in four of all UK deaths. Resistance to current cancer treatments is rapidly increasing meaning there is an urgent need for novel anticancer agents to tackle this crisis. Cancer cells can control what enters the cells through the use of transporters within the cell membranes. These transporters are attuned for specific cargo; thus, efforts are underway to produce anticancer agents which can access this transport system, in a "trojan horse" approach.

A series of molecules have been designed which utilise an amino acid residue, joined through a urea moiety to a known targeting group. The scope of this work is to demonstrate whether the self-association capabilities of these novel compounds can be utilised to disrupt intracellular organelle membranes, with the hypothesis that a lower concentration of compound would be needed to induce a cytotoxic effect to the target cells. This work will also investigate whether amino acid transporters can be used for the influx of compound into the cell.

Poster #13: Genome editing to induce genome rearrangements in a human fungal pathogen

Matt Shaw, University of Kent, Prof Georgios Giamas, University of Sussex, Dr Alessia Buscaino, University of Kent.

Candida albicans a member of the healthy human microbiome and an opportunistic pathogen, causing infections ranging from superficial to systemic. During systemic infection, *C. albicans* can rapidly adapt to any niche in the body and can acquire drug resistance. These traits are partially attributed to its genomic instability, which generates diversity and allows selection of fitter genotypes. This is apparent from the diversity of karyotypes seen in clinical isolates which often have breakpoints around repetitive elements. Such elements include the Major Repeat Sequence (MRS), a repeat array occurring throughout the C. albicans genome. We hypothesise that repetitive elements including the MRS serve as instability hotspots to facilitate genomic rearrangements and rapid evolution. This project aims to establish a cause-and-effect relationship between repeat-associated chromosomal rearrangements and generation of fitter genotypes. To this end, we have used CRISPR-Cas9 to generate double strand breaks within repetitive elements, inducing chromosome rearrangements. These unstable strains have then been phenotyped, and evolved in clinically relevant stresses, including antifungal drugs. Long-read, short read and RNA sequencing have then been used to characterise the novel genotypes and transcriptomes. This has shown that CRISPR-Cas9 can be used to generate different classes of chromosomal rearrangement in *C. albicans*. Strains bearing rearrangements have morphological and fitness changes, as well as reduced pathogenicity during in vivo infection models. This indicates that rearrangements at repeat loci are sufficient to generate phenotypic diversity. Preliminary experiments demonstrate that rearranged strains are also less stable and undergo more frequent karyotype changes during evolution experiments. Further work will look at the effect of this instability on their ability to adapt to stress.

Poster #14: Drug repurposing targeting Mycobacterial respiratory complex - Cytochrome bd

Ryan Boughton, University of Kent, Prof Simon Waddell, University of Sussex, Prof Mark Wass, University of Kent, Dr Mark Shepherd, University of Kent.

Tuberculosis is one of the most widespread and deadliest diseases currently, with a quarter of the global population estimated to be infected with *Mycobacterium tuberculosis* (MTb), and 5 - 10% of these developing symptoms. Antimicrobial resistance is a significant problem with multidrug-resistant MTb increasing in prevalence by approximately 10% a year, new anti-mycobacterial drugs are desperately needed. Alternative to the extremely costly and time-consuming traditional drug development methods, we employ a combination of in silico techniques to identify potential anti-mycobacterial compounds, which are validated by in the laboratory through viability and susceptibility assays. Using *Mycobacterium smegmatis* as a model organism for MTb, we provide first evidence of successful recombinant expression of *M. smegmatis* cytochrome bd into E. coli, enabling purification of M. smegmatis bd. Furthermore, we computationally screened almost 2,000 FDA-approved compounds predicting specific binding affinities against both *M. tuberculosis*, and M.

smegmatis cytochrome bd. The top-ranking compounds were assessed in the laboratory using our newly developed spectrakinetic assay against purified mycobacterial cytochrome bd, identifying new potential anti-mycobacterial compounds.

Poster # 15: Defining the role of factor inhibiting hypoxia-inducible factor-1 (FIH) in the molecular landscape of lung epithelial cells.

Yomna Moqidem, University of Southampton, Institute for Life Sciences, Siyuan Wang, University of Southampton, Kun Zheng, University of Southampton, Chen Yin, University of Southampton, Prof Nullin Divecha, University of Southampton, Dr Andrea Bucchi, University of Portsmouth, Emeritus Prof Donna Davies, University of Southampton, Prof Mark G Jones, University of Southampton, Dr Yihua Wang, University of Southampton,

Idiopathic pulmonary fibrosis (IPF) is a deadly progressive interstitial lung disease in which the lung architecture is replaced by fibrotic tissue and excessive extracellular matrix (ECM) depositions that impair gas exchange. Experimental and clinical evidence strongly points to the role of epithelial cell injury in disease initiation, while the epithelial-mesenchymal crosstalk mediates the disease development and progression. This highlights the importance of unravelling the molecular complexity of epithelial cells. Emerging studies suggest the contribution of hypoxia, and the hypoxia-inducible factor-1 (HIF-1) pathway in disease pathogenesis. Nonetheless, the activity of HIF-1 signaling is regulated by an asparaginyl hydroxylase enzyme called Factor-inhibiting Hypoxia-inducible factor (FIH). While the role of HIF-1 in IPF pathogenesis is well-defined, the role of FIH is under-studied, especially with its ability to hydroxylate other cellular proteins.

This study aims to investigate how FIH regulates the molecular dynamics of alveolar epithelial cells. Specifically, we employed CRISPR/CAS9 and RNA sequencing technologies to determine the impact of FIH knockout on ATII and A549 epithelial cell integrity. Loss of FIH induced both global and cell-specific transcriptomic alterations that lead to various cellular and biological consequences similar to these observed during IPF pathogenesis. Interestingly, our transcriptomic analysis suggests that loss of FIH was sufficient to initiate a pseudo-hypoxic environment, which triggers epithelial-mesenchymal-transition (EMT) across different lung epithelial cells; a leading characteristic phenotype within IPF. This activity was synergised by activating the TGFbeta pathway. Moreover, loss of FIH mediates EMT in alveolar epithelial cells in a mechanism that involves Snail1 upregulation and Smad2 phosphorylation, and this activity was increased in the presence of TGF-beta. Moreover, we report that Snail1 activity during FIH depletion is partially mediated by HIF-1 stabilization.

Collectively, our findings indicate that dysregulated FIH signaling in alveolar epithelial cells might exacerbate epithelial dysfunction by stimulating EMT, which is a profibrotic factor. This suggests FIH as a potential "guardian" protein for alveolar epithelial cells, as its absence precipitates cellular events commonly seen in IPF.

Poster #16: The importance of being integrated: phenotypic integration and its role in domesticability.

Anastasia Kolesnikova, University of Southampton, Dr Rocío Pérez-Barrales, University of Granada, Dr Steven Dodsworth, Birkbeck University of London, Dr Yann Bourgeois, Institut de Recherche Pour le Développement, Prof Mark Chapman, University of Southampton

Domestication and the development of agriculture has been a pivotal point in human history. Domestication was preceded by a long period of human-led cultivation and management of diverse plant species. However, not all the species cultivated ultimately became domesticated - out of the 2500 species that underwent any management, only 250 are considered domesticated.

Why some wild plants were more likely to be successfully domesticated remains unanswered. While many factors may affect whether a species can be domesticated (i.e., its domesticability), the role of phenotypic integration has not yet been explored. Phenotypic integration refers to genetic or physiological relationships between traits in a complex phenotype. More integration between phenotypes that humans saw as beneficial (larger seeds, non-shattering, etc) could speed up selection, and enhance domesticability. Conversely, less integration between beneficial phenotypes could reduce domesticability for never-domesticated wild species.

Chickpea progenitors (those species that were domesticated) and related never-domesticated wild species were grown under six different conditions. Traits related to productivity and competitive ability were assessed. A correlation analysis was undertaken to determine relative integration of phenotypes.

This work contributes to the conversation about whether certain species are predisposed to succeed under certain conditions. It has implications for the neo-domestication and for our understanding of domestication and evolution.

Poster #17: Computational approaches for delineating lysosomal morphological and positional characteristics to elucidate their function

Charles Ellis, University of Southampton, David S. Chatelet, Biomedical Imaging Unit Southampton, David A. Johnston, Biomedical Imaging Unit Southampton, Dr Eloise Keeling, University of Southampton, Prof Louise C. Serpell, University of Sussex, Dr David A. Tumbarello, University of Southampton, Dr J. Arjuna Ratnayaka, University of Southampton, Institute for Life Science, University of Southampton.

Lysosomes are degradative compartments integral to multiple proteolytic processing pathways. The morphological (size, shape) and positional characteristics of lysosomes are indicators of their activity. Morphological changes in lysosomes can affect membrane dynamics, fission/fusion events and cargo/substrate hydrolysis, reported in neurodegenerative diseases as swollen/enlarged lysosomes. Additionally, lysosomal position

is an indicator of functionality, with perinuclear lysosomes associated with high levels of proteolysis. Here, we present several computational approaches to identify morphological and positional features of lysosomes in 2D/3D datasets. Confluent monolayers of the human retinal pigment epithelial cell-line (ARPE-19) were fixed and probed with anti-LAMP2 (lysosomal-associated-membrane-protein-2) to identify mature lysosomes. Images were captured by confocal microscopy using a x63 magnification with system-optimised axial/lateral spacing (Leica SP8). Several programmes were used to develop pipelines and analyse this dataset: Fiji (v2.14.0), CellProfiler (v4.2.8), Icy (v2.5.2.0) Mathematica (v13.3.1) and Python (v6.0.4). Two 2D pipelines (Fiji, CellProfiler), three 3D pipelines (Fiji, CellProfiler, Icy) identified lysosomal size, shape and number. Two novel approaches were created for positional analysis in 2D (Python-HexBin) and 3D (Python, Mathematica). We describe multiple workflows that faithfully delineate morphological and positional features of lysosomes. Given the importance of these characteristics, our next steps will harness these workflows/methods to study lysosomes across neurodegeneration.

Poster #18: Semantic control in episodic memory encoding: an ageing fMRI study

Fiona Lancelotte, University of Sussex, Dr Zara Bergström, University of Kent, Dr Alexa Morcom, University of Sussex

Memory for specific events (episodic memory) declines as people age. An important reason for this decline is that memories are encoded less effectively. In this planned functional magnetic resonance imaging (fMRI) study, we will test how the critical dependence of encoding on prior knowledge differs with age. Despite increased prior knowledge, older adults are less able to use this information flexibly (semantic control) due to reduced integrity of the left inferior frontal gyrus. Competing theories attribute impaired memory encoding either to a fundamental lifespan shift in neural architecture away from frontal brain networks supporting flexible control or to a loss of specialised network architecture. Here, 45 young (20-35 years) and 45 older (65-80 years) adults will encode object images in the scanner using two different strategies, one tapping semantic access and the other also tapping the kind of semantic control which boosts memory in youth. Outside the scanner, participants will be then tested on their memory for these images. We will use advanced multivariate analysis to examine age differences in the regions, multi-region neural activity patterns, and inter-region connectivity involved in successful episodic memory encoding. This foundational research will improve understanding of memory difficulties in healthy older people.

Poster #19: Caught In A TRAP: Characterising The Substrate Binding Protein Vc0430 Of The Poorly Characterised TAXI-TRAP Transporter Family.

Joseph Davies, University of Kent, Nick Massouh, University of Kent, Dr Andrew Daab, University of Kent, Prof Jonathan Essex, University of Southampton, Dr Christopher Mulligan, University of Kent

Tripartite ATP independent periplasmic (TRAP) transporters are widespread in prokaryotes

and are responsible for the transport of a variety of different ligands, primarily organic acids. TRAP transporters are secondary active transporters that employ a substrate binding protein to bind and present the substrate to membrane embedded translocation component. TRAP transporters can be divided into two subclasses; DctP-type and TAXI type, which share the same overall architecture and requirement of the SBP for transport, but their SBPs share no similarity. The TAXI type transporters are relatively poorly understood, with the range of transportable compounds still to be discovered and selectivity requirements for binding unknown. To address these shortfalls in our understanding, we have structurally and biochemically characterized Vc0430 from *Vibrio cholerae* revealing it to be a monomeric high affinity glutamate binding protein. Structural characterization of ligand bound Vc0430 reveals details of the binding site and biophysical characterization of binding site mutant reveal the substrate binding determinants, which differ substantially from the DctP-type TRAPs. To our knowledge, this is the first transporter in *V. cholerae* to be identified as specific to glutamate, which plays a key role in osmoadaptation of *V. cholerae*, making this transporter a potential therapeutic target.

Poster #20: A Role for Talin in Synaptic Plasticity

Natasha Ward, University of Kent, Prof Dan Mulvihill, University of Kent, Prof Kevin Staras, University of Sussex, Dr Christopher Mulligan, University of Kent, Prof Ben Goult, University of Liverpool.

Synaptic plasticity allows the brain to rewire itself in response to everything from learning a new skill to traumatic brain injuries. In the context of learning, removing unnecessary synaptic connections is as vital as creating new ones. However, when these processes go wrong they can have disastrous consequences. Alzheimer's disease (AD), Schizophrenia and temporal lobe epilepsy have all been linked to altered synaptic plasticity. Understanding the mechanisms that allow the brain to choose which connection to enforce and which to prune may be the key to understanding how these diseases develop and ultimately how to treat them. Several hypotheses on how the brain rewires itself have been put forward, including the synaptic tagging and capture hypothesis, which suggests the existence of synaptic tags and plasticity-related proteins. While the identity of these tags has yet to be determined, the mechano-sensitive protein Talin has been suggested as a potential candidate. I will present data on my work on four rare Talin point mutations found in epilepsy patients, establishing the biochemical impact of the altered Talin proteins. I will also present data demonstrating that Talin can bind to the Amyloid Precursor Protein (APP), a protein involved in AD.

Poster #21: Enhancing rAAV Gene Therapy Manufacturing: Improving Productivity and Genome Packaging through Plasmid and Cell Engineering

Oya Isilay Canik, University of Kent, Dr Tim Fenton, University of Southampton, Prof C. Mark Smales, University of Kent.

The use of gene therapy products for the treatment of a large range of genetic indications

and as potential vaccines in the clinic shows great promise, but producing high-titre viral vectors at scale remains a challenge and contributes to the cost of these therapies. The low productivity of fully genome-packaged rAAV (Recombinant Adeno-Associated Virus) from host cells, difficult scalability, and high levels of impurities during bioprocessing of gene therapy medicines in the market show that the current yield of rAAV biomanufacturing falls behind the dosage requirements for both commercial and clinical applications. With a focus on engineering AAV plasmids, we aim to enhance correctly packaged AAV titre and reduce production costs by generating high-yield rAAV constructs. As a priority, pAd-Helper, a low-copy plasmid, was engineered by subcloning E4, E2A, and VA genes into a mammalian expression plasmid to produce a high-copy version for triple transfection experiments with HEK293 cells. After verifying the functionality of the pAd-Helper High Copy Plasmid through ELISA and qPCR assays, the plasmid was used in triple transfection experiments where the RepCap genes were provided in one plasmid, alongside transfection of the helper and genome-containing plasmid flanked by appropriate ITR sequences. Plasmid ratio experiments revealed that transfection with specific ratios (1:1.66:1 and 2.33:2.33:1 for helper:RepCap:genome plasmids) enhanced the genome titre to 1.98E+10 vg/ml and 1.84E+10 vg/ml, and increased packaging efficiency to 11.06% and 9.01%, respectively. Furthermore, Rep2 and Cap2 genes were engineered to create novel variations of pAAV-Rep2/Cap2 plasmids to analyse the role of Rep2 genes (Rep78/68/52/40) and Cap2 genes (VP1/2/3) in AAV packaging to improve rAAV productivity and assess the cytotoxic nature of Rep gene expression on HEK293 cells. Recombinant Rep and Cap protein expression was confirmed by Western blotting, using AAV particles harvested after transfection with engineered Rep and Cap constructs. rAAV packaging efficiency, including capsid formation, genome packaging, and protein expression of Rep and Cap genes, is under investigation through various plasmid ratio transfection experiments.

Poster #22: The effect of caffeine consumption and acute withdrawal on mood, cognition, and resting state brain activity.

Tatum Sevenoaks, University of Sussex, Fiona Lancelotte, University of Sussex, Dr Nick Souter, University of Sussex, Dr Lorenzo Stafford, University of Portsmouth, Dr Charlotte Rae, University of Sussex, Prof Martin Yeomans, University of Sussex.

Few studies have examined how habitual caffeine use and acute withdrawal impact resting-state brain activity. Notably, prior research lacks adequate control for deprivation state, despite evidence that caffeine reinforcement occurs primarily by alleviating withdrawal. This study investigated habitual caffeine use and acute withdrawal, assessing mood, cognition, and resting-state brain activity in three groups: (1) moderate consumers (200–500 mg/day) after overnight abstinence (caffeine-withdrawn, CW); (2) moderate consumers after abstinence followed by 100 mg caffeine (caffeine not-withdrawn, CNW); and (3) non-consumers (<50 mg/day). Sixty participants (n = 20 per group) completed the Bond-Lader mood battery, a rapid visual information processing task, and a resting-state fMRI scan. While no significant group differences emerged for mood and cognition, seed-voxel analysis found significant differences in brain activity. Non-consumers had higher nucleus accumbens to primary visual cortex connectivity and lower connectivity to the lingual and

occipital fusiform gyrus compared to the CW group. Additionally, non-consumers had lower anterior insula to precuneus connectivity compared to the CNW group. These findings suggest that deprivation state alters brain activity in reward-related regions, like the nucleus accumbens. Increased insula connectivity in the CNW group supports caffeine's role in attention. Subsequent independent component analysis is planned to investigate whole-brain differences.

Poster #23: Genomics predicts antifungal siderotype in *P. aeruginosa*

Jacob Hudson, University of Kent, Marta Farre Belmonte, University of Kent, Gary Robinson, University of Kent, Dr Rebecca A. Hall, University of Kent

The Mucorales fungus *Rhizopus microsporus* is a causative agents of mucormycosis, a devastating disease with a rising incidence of 1.7 cases per million globally and a mortality rate as high as 96%. Currently only one drug, amphotericin B, exists as a reliable treatment. Like many microorganisms iron is a key nutrient for *Rhizopus spp*. growth, and previous work has shown that iron chelating pyoverdine type 1 (PVD-1) from *P. aeruginosa* PAO1 has potential as a novel therapeutic. PVD-2 and PVD-3 are produced by other *P. aeruginosa* strains, with the three types sharing a common chromophore and a unique peptide chain granting specificity for its native PVD-Fe importer, FpvA. This raises two questions, do further types exist, and is each type effective against *R. microsporus*? Here we identify the PVD biosynthesis region across all complete genomes in the PGDB, and network analysis reveals three distinct gene sets which type >93% of strains. Type is defined by the peptide chain producing NPRS enzymes, immature PVD exporter, and PVD-Fe importer. The hydrolase and reductase aes and sip are only present in PVD 2 and 3 respectively. Initially, each type appears to be equally antifungal, implying all *P. aeruginosa* strains may be antifungal.

Poster session 4

Poster #24: Exploring the potential of the mitochondria of *Cryptococcus neoformans* as a drug target.

Dmytro Prasolov, University of Kent, Elizabeth Edrich, University of Kent, Prof Anthony Moore, University of Sussex, Eric Pagan, Smiths Medical Inc, Prof. Campbell Gourlay, University of Kent.

Cryptococcus neoformans is an opportunistic fungal pathogen that predominantly affects immunocompromised individuals, causing as many as 181,000 deaths annually. One of the hallmark features of this fungus is its ability to persist within the host in a dormant state for decades. It has been observed that as many as 70% of children in densely populated areas in the USA are exposed to this yeast. The identification of multidrug-resistant strains as early as 1999, coupled with the recent inclusion of C. neoformans in the fungal priority pathogen list by the World Health Organization, underscores the urgent need for new drug development. One potential target for the development of novel drugs is the mitochondria,

which play a central role in vital life processes such as energy production, ergosterol biosynthesis, and iron homeostasis. Unlike human cells, C. neoformans possesses an alternative oxidase system encoded by the AOX1 gene. In many fungal pathogens AOX allows them to maintain mitochondrial function despite oxidative stress. Nitric oxide is of particular interest as it is a compound naturally produced by macrophages to kill pathogens. Here we present evidence of our investigation of Aox1 function in C. neoformans. Our data suggest that Aox1 is important for production of virulence factors such as the capsule as well as for maintain oxidative phosphorylation.

Poster #25: Accessing and recording task-related neuronal activity in the cerebral cortex: using targeted recording configurations.

Shahd Al Balushi, University of Sussex, Alejandra Carriero, University of Sussex, Moira Eley, University of Sussex, Andre Maia Chagas, University of Sussex, Dr Rodrigo Bammann, Scientifica Ltd, Prof Miguel Maravall, University of Sussex.

A principal goal of neuroscience is to determine the mechanisms through which sensory and non-sensory information are encoded during behaviour. Rodents have sophisticated capacities for context-dependent decision-making, and abstraction of sequential rules. We developed an experimental maze to allow mice to express these capacities. The approach aimed to provide robust experimental control while ensuring flexible design of behavioural tasks and being based on accessible components. The maze encourages exploration, while enabling tracking with any machine-vision method). To allow flexible reconfiguration of the maze and the creation of arbitrary associations between stimuli, locations and rewards, standard wall panels can be replaced by devices for reward dispensing or stimulus delivery. Device motion is triggered in real time by animal entry into regions of interest (ROIs); the number of ROIs and maze arms is variable. Mice habituate to the maze within minutes and are intrinsically motivated to explore it with no need for fluid or food restriction. We show that mice learn to navigate to arbitrary locations for rewards. We provide examples of shifts between exploratory/engaged and settled/nestbuilding states. We aim to combine quantification of mouse behaviour and learning performance with recordings of cortical activity using wireless electrophysiological tools.

Poster #26: Environmental and genetic determinants of Brassica crop damage by the agricultural pest Diamondback moth

Shubhangi Mahajan, University of Southampton, Dr Haruko Okamoto, University of Sussex, Dr Stephanie Bird, Royal Horticultural Society, Dr Herman Wijnen, University of Southampton, Institute for Life Science, University of Southampton

Annually, US$4–5 billion is estimated to cost the world economy due to pest infestation of the diamondback moth (DBM), *Plutella xylostella*, due to increasing demand for Brassica over the past two decades. It is one of the most widely distributed lepidopteran species geographically due to its ability to thrive on a broad host range of cruciferous plants, long-distance migration capacity, high resistance to plant (host) defence mechanisms and

insecticides, and strong reproductive ability. This has a significant impact on crop quality and plant survival.

The overarching aim of this study is to investigate environmental and genetic determinants of DBM herbivory in cruciferous plants (*Brassica rapa* and *Arabidopsis thaliana*). Specifically, it will enhance our understanding of factors influencing glucosinolate production in cruciferous host plants and herbivory by the diamondback moth by examining how these processes are impacted by the synthesis of glucosinolates, daily timekeeping of host plants, and light and temperature cycles in the daily environment.

Another objective is to examine changes in gene expression patterns in host plants (*Brassica rapa* and *Arabidopsis thaliana*) and DBM that are closely linked to different levels of herbivory (feeding behaviour) observed in different environmental conditions.

Poster #27: Safeguarding UK hops from *Verticillium nonalfalfae*

Simon Thundow, University of Kent, Dr Helen Cockerton, University of Kent, Dr Andrew Armitage, Natural Resources Institute, Klara Hajdu, Wye Hops, Prof Xiangming Xu, NIAB, Dr Alessia Buscaino, University of Kent.

Annual hop (*Humulus lupulus*) production in the United Kingdom has declined by over 70% since 1981, in part due to the emergence of highly pathogenic strains of the vascular plant pathogen *Verticillium nonalfalfae*, which causes Verticillium wilt disease in hops. Hop cultivars which had previously been considered resistant to Verticillium wilt have since shown susceptibility to the disease in UK hop gardens, suggesting the emergence of resistance-breaking pathotypes. Effector proteins such as VnaSSP4.2 have been discovered in *V. nonalfalfae* affecting hops, but the role that these Secreted Effector Proteins (SEPs) play in the increased virulence of UK pathotypes remains unknown. This study seeks to determine how UK-specific pathotypes of *V. nonalfalfae* have evolved and to identify candidate SEPs involved in the infection of hops.

Through the generation of whole genome assemblies from *Verticillium nonalfalfae* isolates collected from UK hops, we aim to investigate the evolutionary relationships between isolates of different pathotypes through phylogenomic analyses. We then aim to characterise candidate SEPs which may be involved in increased virulence on hop using a bioinformatic pipeline built on genomic, transcriptomic and proteomic studies. This will allow us to determine whether identified genomic variation between pathotypes could be used to develop pathotype-specific diagnostic protocols which may allow rapid in-field identification of virulent strains of *V. nonalfalfae*. Furthermore, by identifying SEPs specific to *V. nonalfalfae* strains we hope to identify new disease control strategies through implementing Host Induced Gene Silencing (HIGS). Overall, this work advances the understanding of how *V. nonalfalfae* causes disease in hops and develops tools to help tackle the disease.

Poster #28: Understanding the Antimicrobial and Antibiofilm Properties of Natural Plant Extracts in the Context of Upper Respiratory Tract Diseases and Health

Iolanta V B Spanner, University of Southampton, Dr Vivien Rolfe, Curiosity Research Ltd, Prof Charles W Keevil, University of Southampton, Associate Prof Sandra A Wilks, University of Southampton.

Biofilms represent the cause of many persistent upper respiratory tract infections (URTIs), which can lead to burdensome healthcare complications and resistance to antimicrobials. This project aims to investigate the antibiofilm properties of various natural plant extracts from herbal teas, how we can enhance our current repertoire of prevention and treatment options with novel approaches. Scanning and Transmission Electron Microscopy indicate drastic changes to the morphology of the bacterial cell membrane of both Haemophilus influenzae and Streptococcus pyogenes, shown by the presence of blebbing (membrane vesicle formation), cell aggregation, loss of cell membrane integrity and a reduction in electron density. Results show consistent antibiofilm activity exhibited by these natural plant extracts, with significant reduction reported on long-established mono-species biofilms after treatment with either Matcha or Raspberry, when compared to control or Chamomile. This demonstrates the ability of plant extracts to cause a significant reduction even against highly established biofilms, which usually exhibit high tolerances for antimicrobials. Additionally, these biofilms have been visualised using Confocal and Episcopic Differential Interference Contrast (EDIC) microscopy, to understand changes to the three-dimensional biofilm architecture under different treatment conditions. Samples were stained to visualise bacterial cell viability (LIVEDEAD) and specific components of the biofilm matrix, including eDNA and glycoproteins (DAPI and Concanavalin A), with results confirming a large presence of dead cells and a change to the biofilm matrix structure after treatment with Matcha or Raspberry. Future work will involve transcriptomics to understand gene expression in response to treatment and HPLC to determine key bioactive compounds.

Poster #29: Investigating the role of Enhancer of Zeste Homolog 2 in a model of age-related cognitive decline

Samuel Liu, University of Southampton, Prof Paul Skipp, University of Southampton, Prof Jessica Teeling, University of Southampton

Alzheimer's Disease (AD) is an age-related disorder causing cognitive decline. Systemic inflammation accelerates disease progression through yet undetermined mechanisms. Enhancer of Zeste Homologue 2 (EZH2) influences expression of the inflammatory pathway TLR4 and is implicated in AD by artificial intelligence algorithms. The aim of this project is to understand modulation of microglia in AD progression by EZH2, and the potential for pathophysiology modification by EZH2 inhibition.

In vivo methods: Tissue from APP/PS1 transgenic mice at 7 and 11 months were collected and processed to investigate EZH2 in neuroinflammation and neuropathology at different stages of disease. Levels of EZH2 and downstream targets' expression and disease progression were quantified using immunofluorescence and qPCR, informing for the creation of a subsequent cohort where EZH2 was pharmacologically inhibited.

In vitro methods: Macrophage-like differentiated THP1 cells were stimulated with LPS and incubated with an EZH2 inhibitor to investigate the consequences of EZH2 inhibition on activated immune cells outside of a model of age-related disorder, informing for subsequent experiments where immune cells are primed by amyloid beta.

We anticipate that this project will develop an understanding of pivotal pathways linking infection, inflammation, and neurodegeneration, thereby advancing our knowledge in cellular mechanisms, and our understanding of health.

Poster # 30: Correlative imaging for fracture prediction in the military

Theo Hornsey, University of Southampton, Prof Julie Greeves OBE PhD, Army Health and Performance Research (AHPR), Dr Jemma Kerns, University of Lancaster, Dr Claire Clarkin, University of Southampton

Awaiting submission of abstract.

Poster #31: Utilisation of bacteriophage-based biofilm community editing techniques for the enhancement of wastewater treatment efficiency.

Matthew Irwin, University of Southampton, Dr Yongqiang Liu, University of Southampton, Juhani Kostiainen, Plant Work Systems, Prof John Williams, University of Portsmouth, Dr Franklin L. Nobrega, University of Southampton, Prof Jeremy S. Webb, University of Southampton.

Wastewater treatment is a globally critical infrastructure for the reclamation of water after human utilisation. Ubiquitous problematic microorganisms within water treatment reactors negatively impact treatment efficiency and can ultimately cause reactor collapse. Problematic glycogen accumulating organisms (GAOs) make consistent phosphorus (P) removal unfeasible and flourish under elevated and rising global temperatures. To combat these current solutions are untargeted and expensive, requiring constant monitoring and modification of operation parameters, impacting long term reactor health. Here, we developed a bioengineering approach harnessing phages for targeted removal of problematic organisms within complex microbial wastewater communities. As a proof of concept, the problematic GAO, *Micropruina glycogenica* Lg2, was selected. We developed an industrial-scale high-throughput virome concentration procedure for collected seasonal viromes from the England's South Coast region. Phage cocktails were introduced to small scale reactors (Pioreactors) to bioengineer a sludge-GAO enriched community, recovering a consistent P removal. The collective potential of bioengineering wastewater could

revolutionise treatment approaches, advancing treatment limits and assist in developing new closed-loop industrial-scale treatment for full nutrient recovery.

Poster #32: Unveiling the role of ApoE in microglial development

Dyuti Basu Choudhury, University of Southampton, Tim A O Muntslag, University of Southampton, Dr Sarah King, University of Sussex, Prof Diego Gomez-Nicola, University of Southampton.

Microglia are the CNS's first responders, surveilling for threats through morphological changes, enabling phagocytosis and protection. They play pivotal roles in brain development and are implicated in Alzheimer's disease (AD) pathogenesis. APOE4 disrupts lipid homeostasis in microglia, leading to inflammation and impaired phagocytosis, and potentially hindering Aβ and tau clearance. Microglial dysfunction associated to APOE4 may manifest during adulthood or in response to challenges, affecting brain health. Previous studies in our lab showed a selective upregulation of APOE expression in microglia during development, specifically around the ages P4-P7. We aim to study whether the presence of the different alleles of APOE (3 vs 4) have different effects on microglia across the embryonic, post-natal and adult ages. Using targeted replacement mice carrying the human APOE3 or E4 alleles, we found an increase in the average density of microglia in the corpus callosum at P7 in E4 mice compared to the E3 mice. Microglia appeared to be less ramified in the adult E4 mice compared to the E3 mice. Dectin-1, which is seen to be expressed by early post-natal microglia, were absent in the E4P7 brain. The next steps would be to analyze the transcriptomics of microglia with the different alleles through single cell RNA sequencing.

10-Minute Talk – Year 4

Presentation Session 1

10-Minute Talk: Coastal rewilding and food security: understanding restoration pathways using ecoacoustics and environmental DNA (eDNA)

Alice Clark, University of Sussex, Dr Ian Hendy, University of Portsmouth, Dr Reuben Shipway, University of Portsmouth, Dr Katie Critchlow, Naturemetrics, Dr Mika Peck, University of Sussex.

Increasing anthropogenic pressures on marine ecosystems, including overfishing, habitat degradation and climate change, are affecting fish communities on a global scale. The decline of marine biodiversity and ecosystem degradation will increasingly harm ecosystem functioning and reduce the provision of essential services for human wellbeing. Fortunately, policy strategies aimed at protecting and restoring marine biodiversity are increasing. In 2021, the Nearshore Trawling Byelaw was introduced by the Sussex Inshore Fisheries and Conservation to protect 300km2 of the Sussex coastline from bottom trawling. The Byelaw aims to protect essential fish stocks and protect important coastal marine habitats, such as

kelp beds. In this study we assessed the effectiveness of the Byelaw by monitoring marine biodiversity using Baited Remote Underwater Videos and environmental DNA metabarcoding. Although there hasn't been a significant change in the number of species detected each year, we have created a baseline of the species present in Sussex. We have also found that the fish communities in Sussex are structured by depth, tidal rate, treatment and year. The results from this study provide a crucial foundation for future biodiversity monitoring as the ecosystem recovers following the removal of trawling pressure. Long-term monitoring will be essential to track ecological changes, assess recovery trajectories and inform adaptive management strategies.

10-Minute Talk: Development of novel small molecule inhibitors of Tyro3 receptor tyrosine kinase

Austeja Bakulaite, University of Portsmouth, Abdulkareem Ayfan, University of Portsmouth, Damien Crepin, University of Sussex, Karen Ball, University of Portsmouth, Prof John Spencer, University of Sussex, Prof Paul Cox, University of Portsmouth, Dr Sassan Hafizi, University of Portsmouth

Tyro3 is a member of the TAM subfamily of receptor tyrosine kinases (RTKs), which are involved in promoting cell proliferation, migration, and suppression of anti-tumour immunity. Tyro3 is overexpressed across different tumours and is associated with poor patient prognosis. Currently, there are no clinically approved selective Tyro3 inhibitors as anti-cancer therapeutic agents. Our research aims to discover novel small molecules as selective inhibitors of Tyro3 kinase for eventual subsequent drug development for Tyro3-dependent cancers.

Previous work from our group using molecular docking analysis has identified several small molecules that virtually occupy the kinase ATP-binding pocket of Tyro3. Currently, we are working to test these hits as potential Tyro3 kinase inhibitors using computer-based and experimental models.
The top hits in the docking analysis are subsequently being tested in vitro in a kinase activity assay against Tyro3 kinase activity and against other TAMs. Additionally, we are testing them in cell-based assays, such as cell viability and apoptosis assays. Furthermore, novel molecules similar in structure to the docking hits have been synthesised, which we are also currently testing.

From these combined analyses, the most promising compounds for Tyro3 inhibitory potency and selectivity will be further investigated in wider kinome screening.

10-Minute Talk: Manipulation of chloroplast density to enhance photosynthesis and nutritional value of tomato.

Erick Oliveira, University of Southampton, NIAB, Prof Matthew J. Terry, University of Southampton, Dr Andrew J. Simkin, NIAB, University of Essex.

As global population growth continues to put pressure on existing agricultural systems, improving photosynthetic efficiency becomes ever more important to achieve sustainable food security. The ability of crop plants to convert light energy into chemical energy to sustain growth is achieved by chloroplasts. In fruits, chloroplasts are converted to chromoplasts during ripening, and this is associated with chlorophyll degradation and carotenoid accumulation. The genetic manipulation of fruit chloroplasts could simultaneously improve both photosynthetic capacity and, fruit size, as well as fruit quality traits. This study explores the genetic manipulation of chloroplast development and density in tomato (*Solanum lycopersicum*) to enhance pigment content, photosynthesis, and overall fruit quality. To achieve that, we identified target genes for the manipulation of chloroplast development. The expression of a birch MADS-box gene in tobacco enhanced chloroplast growth and division and increased photosynthetic rates by 2-fold. Expression of the Arabidopsis transcription factor CGA1 also increased chlorophyll content and enhanced photosynthetic efficiency. Both approaches also led to higher accumulation of the carotenoids, lycopene and β-carotene suggesting an improvement in fruit quality. The technology proposed in this project represents an important milestone in the genetic manipulation of fruit photosynthesis and could be utilised in other fruit crops.

10-Minute Talk: Investigating the effect of PURA missense variants on neurodevelopment in X. tropicalis frogs using CRISPR base editing

Sophie Powell, University of Southampton, Prof Diana Baralle, University of Southampton, Dr Gabrielle Wheway, University of Southampton Prof Matt Guille, University of Portsmouth.

PURA encodes a single-stranded nucleic acid-binding protein, de novo variants in which are responsible for PURA syndrome, a severe neurodevelopmental disorder. Pathogenic variants span the length of the Purα protein, but no strong correlation has yet been found between the type and localisation of these variants and the presence or penetrance of clinical features in patients, limiting prediction of patient prognosis and the scope of therapy design.

Xenopus frogs have been estimated to share over 80% of all human disease genes, including PURA. Knockout of the frog pura gene in Xenopus tropicalis by our group produces a clear neurodevelopmental phenotype similar to the human disease, affecting morphology, survival and working memory of both crispant and F1 tadpoles. To determine their effect on neurodevelopment, PURA missense variants from genomic databases and the literature will be precisely recreated in *X. tropicalis* frogs using CRISPR base editing.

To do this, a base editor with a more permissive PAM will first be created and optimised for use in Xenopus. Base-edited tadpoles possessing patient missense variants will then be created and their development and behaviour characterised. This will further our understanding of the relationship between variant localisation and severity of phenotype in PURA syndrome.

10-Minute Talk: Investigating metabolic dysfunction as a driver of Motor Neuron Disease

Fiona Dresel, University of Kent, Prof Majid Hafezparast, University of Sussex, Dr Campbell Gourlay, University of Kent.

Awaiting submission of abstract.

Presentation Session 2

10-Minute Talk: Developing an in vitro model of liver zonation

Amanda Gilbert, University of Southampton, Charley Duffell, University of Southampton, Bram Sengers, University of Southampton, Simon Lane, University of Southampton, Dr Jonathan West, University of Southampton, Dr Nicole Prior, University of Southampton

The liver is involved in diverse, often contrasting physiological roles including detoxification of substances, protein synthesis and glucose metabolism. To maintain efficiency, opposing functions are spatially separated through zonation of its main functional cell, hepatocytes. A key driver of zonation is thought to be oxygen availability. As oxygenated blood flows from the hepatic artery towards the central vein, an oxygen gradient of 8.5-4% is formed, shaping the microenvironment of hepatocytes. Hepatic zonation can be split into three areas: the periportal zone, found closest to the portal vein and hepatic artery, the pericentral zone located next to the central vein, and the mid-lobular zone, between the two. Production of accurate, high fidelity in vitro models provides opportunities for the development of new treatments for liver disease, generation of material for transplantation and improved toxicity screening. Current 2D and 3D models often fail to recapitulate the zonated liver and are unable to generate fully mature hepatocytes. Guided by computational modelling, oxygen availability to hepatocyte organoids has been altered through changing medium heights with the aim to produce an in vitro model of liver zonation.

10-Minute Talk: Computational predictions of thermostability and binding affinity changes in enzymes

Konstantinos Tornesakis, University of Portsmouth, Prof Jonathan W. Essex, University of Southampton, Dr Gerhard Koenig, University of Portsmouth, Prof. Andrew Pickford, University of Portsmouth, Prof Paul Cox, University of Portsmouth.

Enzymatic recycling of PET plastic requires enzymes with high stability at high temperatures. IsPETase degrades PET polymers at ambient temperatures. HotPETase, designed with directed evolution, is a thermotolerant variant of IsPETase able to degrade PET at 65 degrees. In this project, experimental and computational approaches were used to investigate the stability of these two enzymes, as well as their intermediates. Protein unfolding was studied with differential scanning calorimetry. Activation energy and activation temperature showed an increase during the evolution process. HotPETase and one predecessor (M10-HP) displayed increased thermodynamic properties. The PET

degradation rates of all enzymes revealed different kinetic stabilities. The optimum temperature for activity was increased from IsPETase to HotPETase. HotPETase showed less degradation yield compared to M10-HP at 65 degrees. Binding of PET to the active site was investigated with molecular docking calculations. The best docked poses were further refined with molecular dynamics simulations to account for flexibility and temperature effects. Trajectory analysis of the molecular dynamics simulations of the variants indicated the probability of PET obtaining the optimum distances within the active site. Finally, for simulations at 60 degrees, HotPETase and M10-HP were found to have probability of obtaining the necessary distances, whereas IsPETase was incapable of.

10-Minute Talk: Targeting myosin-X to promote axon regeneration following spinal cord injury

Mathew Davis-Lunn, University of Southampton, Dr Ben Goult, University of Liverpool, Prof Melissa Andrews, University of Southampton.

Following spinal cord injury (SCI), functional recovery is limited by the inability of damaged central nervous system axons to regenerate. Integrin receptors mediate adherence of these axons to the extracellular matrix (ECM), and subsequent outgrowth, providing an established therapeutic target. Inhibitory ECM molecules upregulated after SCI impede axon regeneration, in part by inactivation of integrin receptors.

Our primary aim is to enhance methods of integrin-mediated axon regeneration. This talk will focus specifically on myosin-X, which colocalises with active integrin receptors in filopodia. We test the ability of myosin-X overexpression to enhance neurite outgrowth of PC12 pheochromocytoma cells, differentiated on combinations of permissive and inhibitory ECM substrates.

We show that myosin-X expression significantly enhances neurite outgrowth in PC12 cells differentiated on an inhibitory ECM. Our results indicate a synergy between the expression of specific integrin receptors and myosin-X for neurite outgrowth in vitro. Targeting myosin-X therefore provides a promising approach for the enhancement of integrin-mediated axon regeneration in vivo.

10-Minute Talk: Growing complimentary crops and nutritionally rewarding cultivars to sustain insect pollinators and crop pollination on farms

James Woodward, University of Sussex, Dr Michelle Fountain, NIAB East Malling, Prof Dave Goulson, University of Sussex.

About 70% of crop plants grown globally rely to varying degrees on insects for pollination. These crops are responsible for 35% of worldwide food production and an estimated €153 billion of global food production would have been lost in 2005 if pollinating insects were absent. Wild pollinators have declined in abundance and diversity in Northwest Europe and North America. Optimising pollination for pollinator-dependent crops is of great value to

society as these crops produce many fruits, vegetables, seeds, nuts and oils which contribute towards healthy human diets. Therefore, identifying strategies to mitigate pollination deficits is of international importance. An approach to boost pollinators and pollination on farmland is to develop complementary cropping systems where sequentially flowering pollinator-dependent crops extend the period of forage availability for pollinators. This strategy could be further enhanced by identifying crop cultivars which are highly nutritious and attractive to pollinators. Identifying nutritious crop cultivars involves quantifying the nutritional quality of the floral resources nectar and pollen. Nectar mainly provides a source of carbohydrates, whereas pollen predominantly supplies proteins, lipids and micronutrients. This project investigates whether pollination deficits could be mitigated on farmland by selecting nutritious and attractive crop cultivars for complementary cropping systems.

Presentation Session 3

10-Minute Talk: Biophysical characterisation of recombinant *E. coli* vesicles

Bree Streather, University of Kent, Gregory Mashanov, The Francis Crick Institute, Dr Jennifer Hiscock, University of Kent, Prof Jonathan Essex, University of Southampton, Prof Dan Mulvihill, University of Kent

Eastwood et al. (2022) describes an innovative peptide tagging based technology that allows the production of diverse recombinant proteins in *E. coli* that are subsequently packaged into membrane-bound vesicles and exported into the media. This has many advantages including simplified downstream processing and storage. It has also been shown to significantly increase yield of particularly challenging or insoluble proteins. Recent work to determine the biophysical characteristics of the vesicles has included experiments to determine the average size of the vesicles and the number of recombinant protein fusions inside the vesicles. This has provided vital insight into the mechanism of action and the efficiency of the expression system. Alongside this, co-expression of a VNp-fusion with a membrane protein termed MAV (Membrane Activated Vesicles) for the purpose of functionalising the surface of the vesicles has been examined. Is it possible to express a protein of interest in the lumen of a vesicle with a membrane protein coating the outer surface? What is the efficiency of this co-expression and what is the effect on overall protein expression? These are the questions that will be explored in my talk.

10-Minute Talk: Which one smells nicer? : Host plant preference of Meadow spittlebug (*Philaenus spumarius*) feeding on lavender varieties in the UK

Susmita Aown, University of Sussex, Dr Michelle Fountain, NIAB, Dr Hayley Jones, Royal Horticultural Society (RHS), Prof. Alan Stewart, University of Sussex

Meadow Spittlebug, *Philaenus spumarius*, a sap-sucking insect herbivore, is the most important vector in southern Europe of *Xylella fastidiosa*, a bacterial pathogen causing Pierce's disease in various plants. *P. spumarius* is widespread in Britain and is often abundant on lavender (Lavandula spp.) grown commercially for its essential oil. *X. fastidiosa*

has not been detected in the UK, but *P. spumarius* would be an important vector, and lavender could be highly susceptible to the bacterium if the pathogen were introduced. We sampled four commercially grown varieties (*L. angustifolia* varieties Maillette, Folgate & Ladybird and *L. x intermedia* variety Grosso) in a lavender nursery and a lavender farm setting. The abundance of nymphs (as the number of spittle masses) and adults (by sweep netting) were quantified on randomised plants along planted lavender rows. *P. spumarius* nymph and adult density was significantly higher on *L. angustifolia* than on *L. x intermedia*. All three *L. angustifolia* varieties supported high nymphal density, but the adult density was significantly low on the variety Ladybird. Our results showed that *P. spumarius* differentiated between lavender species, but there was no clear evidence of varietal preference within the same lavender species. These results indicate that if *X. fastidiosa* entered the UK in the future, *L. angustifolia* could be at risk. Furthermore, because of its popularity as a garden plant, it could also act as a significant reservoir for the pathogen.

10-Minute Talk: How does Lipiodol affect the endometrium?

Molly Rutt, University of Southampton, Dr Alexandra Kermack, University of Surrey, Frimley Health Foundation Trust, Dr Sachin Modi, University Hospital Southampton NHS Foundation Trust, Dr Bonnie Ng, University of Southampton, University Hospital Southampton NHS Foundation Trust, Dr Linden Stocker, University Hospital Southampton NHS Foundation Trust, Ella Proudley, University of Southampton, Prof Sarah Newbury, University of Sussex, Prof Rohan Lewis, University of Southampton, Prof Ying Cheong, University of Southampton, University Hospital Southampton NHS Foundation Trust, Dr Jane Cleal, University of Southampton

Hysterosalpingogram (HSG) is a common fertility investigation for those struggling to conceive. During this scan, an iodinated contrast agent is inserted into the womb, which can be visualised via x-ray as it fills the uterine cavity and passes through the fallopian tubes. This allows identification of any structural disorders/pathologies in the womb or blockages in the fallopian tubes.

HSG has also been shown to help women fall pregnant, and use of Lipiodol, an oil-based contrast agent, results in significantly higher pregnancy rates compared to other contrasts.

24 women were recruited and consented to sampling of their endometrial tissue and fluid on day 21 of their menstrual cycle, both before HSG and 1 month after.
Endometrial tissue lipid levels were analysed via gas chromatography. Extracellular vesicles were purified from endometrial fluid and analysed via flow cytometry. Transcriptomic analysis was performed on vesicle-associated microRNA, and tissue micro and mRNA.

Endometrial tissue phosphatidylcholine levels were significantly elevated following HSG (72% increase from 2.3 mg/g to 4.0 mg/g. n=8, p= 0.031). Extracellular vesicle number was significantly reduced by 28% after HSG (n=12, p=0.045). No significant differences in m/miRNA expression were observed; vesicle-associated miRNA is currently being analysed.

Lipiodol may mediate an increase in pregnancy rates via modulating the endometrial tissue lipid composition or secretion of extracellular vesicles. Short-term effects of lipiodol will be investigated via endometrial organoids and attempt to characterise the mechanism of action.

10-Minute Talk: Does the GluN2A subunit contribute to NMDAR activity in layer 5 pyramidal neurons in the mouse prefrontal cortex in health and disease?

Oreoluwa Fakeye, University of Southampton, Dr Andrew Penn, University of Sussex, Dr Mariana Vargas-Caballero, University of Southampton.

The prefrontal cortex (PFC) is important for working memory and its dysfunction is implicated in schizophrenia. Inhibiting NMDA receptors (NMDARs) in primates performing behavioral tasks reduces working memory-associated neuronal activity in the PFC. NMDARs are tetramers, formed of two obligatory GluN1 subunits paired with identical (diheteromeric) or different (triheteromeric) GluN2/GluN3 subunits.

Slow decaying GluN2B mediated currents sustain the recurrent activation of layer V pyramidal neurons in the mouse PFC, underlying working memory. GluN2A truncations are associated with Schizophrenia. However, research on their effect on working memory focuses on interneurons due to the perceived dominance of GluN2B in pyramidal neurons.

Here, I show a developmental acceleration of the NMDAR decay kinetics in layer V pyramidal neurons indicative of a developmental GluN2A subunit incorporation in the mouse PFC. Following this developmental acceleration, the NMDAR decay kinetics are still slower decaying in the mouse PFC than in a sensory area (Primary somatosensory cortex).

This is significant because it shows that the GluN2A subunit is involved in the recurrent activation of NMDA receptors in the mPFC possibly by its incorporation into triheteromers. In Schizophrenia, the loss of GluN2A may lead to increased recurrent activation which may underlie some of the disease symptoms. My future work will address this.

10-Minute Talk: Structural and functional characterisation of the *E.coli* DedA protein YqjA

Tom Paige, University of Kent, Dr Christopher Mulligan, University of Kent, Aline Le Roy, ISBG, Dr Vanessa Leone, NIH, Dr Lucy Forrest, NIH, Dr Mark Paget, University of Sussex.

The maintenance of membrane homeostasis in bacteria is essential for the several key physiological processes including cell division, nutrient uptake and antimicrobial resistance mechanisms. Membrane homeostasis requires the synthesis and distribution of lipids. However, the transporters for most major lipid species are not known. The DedA superfamily of integral membrane proteins are widespread in bacteria and recent studies have shown that DedAs are lipid transporters. Notably, this lipid flipping activity is key to antimicrobial resistance, with DedA knockout mutants becoming susceptible to several antibiotics in clinically relevant pathogens. Therefore, the DedA family is a prime target for

the development of inhibitors to sensitize resistant pathogens. Currently, we have limited data on the structure of DedA proteins and their lipid transport mechanism, essential information for developing inhibitors.

Here, we have characterised the oligomeric state of the model DedA protein, YqjA from E. coli, revealing it to be a dimer, and experimentally validated the dimeric interface. Using a liposome-based lipid flipping assays we have characterised YqjA's lipid flipping activity revealing that it can flip both of the major lipid species in *E. coli*, PE and PG. This work reveals important mechanistic insight into a transporter family central to bacterial physiology.

Presentation Session 4

10-Minute Talk: KlebPhaCol: A community-driven resource for Klebsiella research identified a novel gut phage order associated with the human gut

Daniela Rothschild-Rodriguez, University of Southampton, Kai Lambon, University of Southampton, Agnieszka Łątka, Ghent University, University of Wroclaw, Ana Rita Costa, Delft University of Technology, Claire King, University of Southampton, Dimitri Boeckaerts, Ghent University, Elizabeth Sheridan, University Hospitals Dorset NHS Foundation Trust, Francis Drobniewski, Imperial College London, Ilaria De Angelis, Ghent University, Kordo Saeed, University of Southampton, University Hospital Southampton NHS Foundation Trust, Macy Martin, University of Southampton, Mark Sutton, United Kingdom Health Security Agency, Matthew Wand, United Kingdom Health Security Agency, Michael Andrew, University of Southampton, Morgen Hedges, University of Southampton, Stan J. J. Brouns, Delft University of Technology, Peter Weigele, New England Biolabs, Pieter-Jan Haas, University Medical Center Utrecht, Simran Krishnakant Kushwaha, University of Southampton, Sophie Lawson, United Kingdom Health Security Agency, Yan-Jiun Lee, New England Biolabs, Yves Briers, Ghent University, Dr Jessica Teeling, University of Southampton, Dr Jerome Swinny, University of Portsmouth, Dr Franklin L. Nobrega, University of Southampton, Institute for Life Science, University of Southampton

The clinical importance of *Klebsiella pneumoniae*, a pathogen associated with highly antibiotic-resistant infections and gut colonization, has intensified interest in alternative treatments, including bacteriophages. While increasing numbers of Klebsiella-targeting phages are being studied, their therapeutic applications are still limited, partly due to limited access to phage-bacteria pairings, which hinders centralised knowledge expansion. To address this, we created the open-source Klebsiella Phage Collection (KlebPhaCol), containing 53 phages and 74 Klebsiella isolates that we comprehensively characterised. These phages can target 27 sequence types, including clinically relevant ST258, ST15, ST14, ST23, ST17, ST86, ST11, and ST323, and 28 capsular types, such as the highly virulent KL1 and KL2. The collection includes phages from five distinct families – one of which belongs to a novel identified phage order, Felixvirales, associated with the human gut – while the strains span six Klebsiella species. We envision KlebPhaCol as a valuable, reference resource to advance research on Klebsiella-phage interactions, extending beyond phage therapy. The

collection has been shared with 21 labs across eight countries so far and is freely available at www.klebphacol.org, supporting collaborative research worldwide.

10-Minute Talk: Identification of determinants of virus phenotypes, including SARS Coronavirus-2/COVID-19

Hannah Uri, University of Kent, Prof Martin Michaelis, University of Kent, Dr Christopher McCormick, University of Southampton, Dr Mark Wass, University of Kent.

Awaiting abstract submission

Presentation Session 5

10-Minute Talk: Defining Solutions for the Improvement of Food Security in the UK: Parsnips as a Case Study for Dietary Intervention

Annabelle Somers, University of Southampton, Dr Jenny Baverstock, University of Southampton, Prof Guy Poppy, University of Bristol, Dr Eleftheria Stavridou, NIAB, Prof Philip Calder, University of Southampton, Dr Frances Gawthrop, Tozer Seeds Ltd.

The UK is facing a public health crisis, with poor diet contributing to a range of chronic diseases, including heart disease, mental health issues, and poorer pregnancy outcomes. A key aspect of this dietary issue is folate deficiency, with one in six UK teenagers clinically deficient in this essential micronutrient. Folate plays a critical role in cellular metabolism and gene expression and is associated with the prevention of several conditions, including colorectal cancer and folate-deficiency anaemia. This study investigates the potential of parsnips, a vegetable high in folate, as a solution to improve dietary folate intake in the UK. Early findings show a 3.5-fold variation in folate content across different parsnip varieties, suggesting that selecting more nutrient-dense varieties could significantly boost folate intake. Additionally, parsnips retain their folate content even after prolonged storage, making them a stable and viable source of this micronutrient. Incorporating parsnips into school meal programmes could provide an affordable and effective strategy for improving folate intake among young people. This research highlights the potential of parsnips as a cost-effective, sustainable solution to combat folate deficiency in the UK, with implications for public health policy and dietary intervention.

10-Minute Talk: Understanding sexual dimorphism in appetite and mating behaviours

Noviann McLean, University of Kent, Yasir Malik, University of Kent, Justin De Araujo, University of Kent, Lydia Bennett, University of Kent, Minaxi S. Gami, University of Kent, James Evans, University of Kent, Nathan Dennis, University of Kent, Dr Marina Ezcurra, University of Kent, Dr Kieran Edwards, Sibelius Natural Products, Dr Jennifer M. A. Tullet, University of Kent

Sexual dimorphism is essential for optimizing survival and reproductive success. C. elegans hermaphrodites and males employ distinct strategies to balance nutrient acquisition, find food, and mate. Hermaphrodites must allocate energy efficiently between food intake, reproduction, and survival, whereas males prioritize mate-seeking and exploratory behaviours.

The SKN-1/Nrf transcription factor family is integral to metabolic homeostasis, oxidative stress resistance, and detoxification. In C. elegans, SKN-1B, is expressed in the two chemosensory ASI neurons where it acts to control hermaphrodite exploratory behaviours, satiety responses and mitochondrial homeostasis.

Here, we show that SKN-1B/Nrf displays a sexually dimorphic expression pattern and regulates whole-body gene expression differently in hermaphrodites and males. Moreover, SKN-1B/Nrf influences mitochondrial network integrity and bioenergetic states as well as a wide range of physiological and behavioural phenotypes (including those involved in food-seeking and mating behaviours) in a sex-specific manner. Our findings establish SKN-1B as a critical regulator of sexually dimorphic metabolic and behavioural traits, and demonstrate its role in coordinating feeding and reproductive strategies. This work provides new insights into neuronal regulation of metabolism and behaviour, with implications for sex-specific physiological adaptations in other species.

10-Minute Talk: Exploiting *Mycobacterium tuberculosis* biofilm-derived phenotypes for novel drug-target discovery

Kaya Taylor, University of Sussex, Prof Jeremy Webb, University of Southampton, Dr Joanna Bacon, UK Health Security Agency, Dr Simon J Waddell, University of Sussex.

Mycobacterium tuberculosis (M.tb) is the causative agent of tuberculosis (TB), the WHO estimated that 7.5 million people fell ill with TB in 2022 and 1.3 million people died from active disease. Lengthy and toxic drug therapies are hampering efforts to control this disease, as is the emergence of antibiotic drug resistance. Therefore, the introduction of new drug regimens using novel drugs is fundamental to eradicating this disease.

M.tb has been observed to grow as aggregated clumps or clusters of bacilli both in vitro and in lung tissue, as a single organism biofilm. This aggregated biofilm-like growth causes changes to the phenotype of the bacilli, inducing phenotypic heterogeneity that may impact antimicrobial drug efficacy. Here, we describe the development of an M.tb biofilm model to mimic aggregated extracellular growth in lung lesions and to measure drug action using a luciferase reporter system alongside 16s RNA and CFU. Biofilm-derived M.tb exhibited tolerance to first line drugs including rifampicin, ethambutol, isoniazid and bedaquilline. There were further increases in drug tolerance observed between different media conditions, such as a decrease in pH and supplementation with cholesterol.

Identifying and characterising drug-tolerant M.tb populations will improve our

understanding of the action of drugs in vivo and may help advance novel treatment-shortening drug regimens for TB.

10-Minute Talk: Investigating the Role of 5-HT Receptor Subtypes in the Modulation of Cell-Specific Immune Function

Jamie Thomas, University of Southampton, Prof Diego Gomez-Nicola, University of Southampton, Dr Gary Gilmour, COMPASS Pathways, Dr Maqsood Ahmed, COMPASS Pathways.

5-Hydroxytryptamine (5-HT) is a conserved biogenic monoamine that can act as a neurotransmitter, hormone, and mitogen across multiple biological systems. 5-HT signalling is primarily mediated by the family of 5-HT receptors (1-7), which comprises 15 known mammalian subtypes. Emerging evidence shows that most immune cells express one or more 5-HT receptor subtypes, while numerous immunological functions have been linked to 5-HT signalling, which suggests a key role in the immune system. To date, the full extent of 5-HT receptor expression within immune cells, alongside the influence that these different receptor subtypes have on immune cells remains relatively unknown. In this project, we aim to utilise a range of techniques to 1) investigate the expression of 5-HT receptor subtypes in murine immune cells, 2) characterise the immunomodulatory functions associated with 5-HT signalling, and 3) identify if these functions can be manipulated using known pharmalogical tools. Together, this work will advance our understanding of 5-HT signalling in the immune system and may offer new insights into how immune processes are regulated under physiological conditions and in diseased states, from a serotonergic signalling stand point.

10-Minute Talk: Pesticide Selectivity: Exploring a novel target in *Caenorhabditis elegans*

Henry Nvenankeng, University of Southampton, Debayan Sarkar, Syngenta, Jim Goodchild, Syngenta, Philippa Harlow, Syngenta, Prof Lindy Holden-Dye, University of Southampton, Prof Vincent O'Connor, University of Southampton

Nicotinic acetylcholine receptors (nAChRs) are fast acting ligand gated ion channels that have been widely investigated in vertebrate and invertebrate organisms for selective targets to chemically control insect pests in agriculture and veterinary medicine. Here, we investigate EAT-2, a nAChR that regulates feeding behaviours in the nematode *Caenorhabditis elegans* as a novel druggable target for mitigating parasitic worms. Its uniqueness among nAChR as they lack key vicinal cysteine residues that are essential for ligand binding, its dependence on EAT-18, an auxiliary protein with no known orthologs for functional expression, and a phylogeny that reveals conservation within the Nematoda suggest possibilities as a novel, selective pharmacophore. In plant parasitic nematodes (PPNs) pharmacological data are consistent with EAT-2 regulating stylet thrusting, the parasitic behaviour required for root invasion, feeding and hatching of juveniles. Using *C. elegans* as a surrogate model animal in a bioassay to screen for EAT-2 selective compounds, we have identified modulators of the receptor. In a recombinant assay, we expressed EAT-2

in frog oocytes and validated the identified modulators as antagonists of EAT-2. When tested on infective juveniles of the PPN *Globodera rostochiensis*, they inhibited stylet thrusting with varying potencies and could be significant in disrupting host plant invasion and potentially break parasitism.

Presentation Session 6

10-Minute Talk: Developing novel approaches for time-resolved serial crystallography

Jack Stubbs, University of Southampton, Prof Ivo Tews, University of Southampton, Dr Jonathan West, University of Southampton, Dr Allen Orville, Diamond Light Source, Dr Pierre Aller, Diamond Light Source, Patrick Shaw-Stewart, Douglas Instruments, Stefan Kolek, Douglas Instruments, Dr Mark Roe, University of Sussex

Recent advances in structural biology are revolutionising our understanding of biomolecular processes. Capturing structural changes over time allows for detailed investigations of ligand binding and enzymatic reactions. Time-resolved serial crystallography, utilising thousands of microcrystals to generate composite datasets, is particularly powerful for studying protein dynamics.

However, preparing well-defined microcrystalline samples remains a challenge, as no universal crystallisation method suits all proteins. Reliable techniques for growing and handling such tiny crystals are essential for obtaining high-quality structural data. We have developed a robust workflow to optimise crystal growth for size and uniformity, combining microseeding and phase diagram approaches in collaboration with Douglas Instruments, alongside high-throughput droplet microfluidics developed at Southampton.

Efficient sample delivery is equally crucial. To address this, we have designed a droplet microfluidic platform that exploits convection within droplets for rapid ligand mixing. In collaboration with Diamond Light Source, we have implemented a fast-shutter system at X-ray free electron laser (XFEL) facilities, capturing ultrafast molecular events, including the conformational switch in the iron-binding protein FutA.

These advancements enhance our ability to resolve biomolecular mechanisms at unprecedented resolution, paving the way for breakthroughs in medicine and drug discovery.

10-Minute Talk: Predicting novel drug targets that are synthetically lethal vs. SMAD4 loss

Joanna Renaut, University of Sussex, Dr Ajay Mistry, Oppilotech, Dr John George, Oppilotech, University of Leeds, Dr Helfrid Hochegger, University of Sussex, Dr Frances MG Pearl, University of Sussex

Cancer is the leading cause of death in the majority of countries. Therapeutic options have improved in recent decades, yet certain cancers remain difficult to treat. In 2014, Cancer

Research UK highlighted oesophageal, lung, brain, and pancreatic cancers as cancers of unmet need, necessitating improved therapeutic strategies.

SMAD4, a tumour suppressor frequently mutated in challenging cancers, has proven difficult to target therapeutically. Synthetic lethality (SSL) emerged as a promising strategy, notably following its 2005 application in BRCA1/2-deficient cancers. Known SSL partners for SMAD4 in colorectal cancer include BET proteins (BRD2, BRD4), AURKA, KLF5, and recently, RAB10.

In this study, I combined computational and experimental methods to identify novel SSL dependencies with SMAD4 loss in the four cancers of unmet need. Robust statistical analyses predicted new SSL targets, validated experimentally through CRISPR knockout and siRNA depletion assays assessing cell viability.

Our work validated three novel synthetic lethal interactions with SMAD4, previously unreported in literature. These discoveries offer potential new therapeutic avenues and hope for improving outcomes in cancers with limited treatment progress.

10-Minute Talk: Control of *Listeria monocytogenes* biofilms in the fresh food supply chain

Lucy Sutton, University of Southampton, Dr Callum Highmore, University of Southampton, Innogen Carter-Hall, Vitacress, Assoc Prof Sandra Wilks, University of Southampton, Prof Charles William Keevil, University of Southampton

Listeria monocytogenes is an opportunistic food-borne pathogen that can survive under harsh conditions such as refrigeration temperatures, low oxygen levels and low nutrient levels – therefore is a problem in the fresh food supply chain. Infection with *L. monocytogenes* can result in listeriosis, potentially fatal in those with a weakened immune system. This study aims to evaluate the efficacy of common sanitisation methods used in the fresh food supply chain, using appropriate laboratory models of Listeria biofilms. *L. monocytogenes* Scott A, *L. monocytogenes* CECT 936 and *L. innocua* biofilms were grown at 20°C or 4°C, on stainless steel coupons for 7 days, and treated with high concentrations of chlorine (up to 300 ppm) or peracetic acid (up to 500 ppm) on days 1, 3, 5, and 7. Coupons were then processed for culturable cell counts, EDIC/EF microscopy, CLSM, and Raman spectroscopy. The results of this study show that temperature effects biofilm growth, as biofilms reached ~108 CFU/cm2 at 20°C, but were significantly lower at 4°C (~104 CFU/cm2). Both treatments were shown to be effective at treating Listeria in the planktonic form, but were not effective at treating biofilms. Raman spectroscopy did indicate a physiological response to treatment, and future work would investigate the stress response at the molecular level using transcriptomics. This work provides important information on sanitisation efforts in the fresh food supply chain, concerning surface material, factory temperature and age of biofilm.

10-Minute Talk: Structural insights into anaerobic-based multidrug resistance by the efflux pump MdtF

Ryan Lawrence, University of Southampton, Mohd Athar, University of Cagliari, Muhammad R. Uddin, University of Oklahoma, Christopher Adams, UCB Pharma, Joana Sousa, UCB Pharma, Oliver Durrant, UCB Pharma, Sophie Lellman, UCB Pharma, Lucy Sutton, University of Southampton, Prof Charles W. Keevil, University of Southampton, Nisha Patel, UCB Pharma, Christine Prosser, UCB Pharma, David McMillan, UCB Pharma, Helen I. Zgurskaya, University of Oklahoma, Attilio V. Vargiu, University of Cagliari, Zainab Ahdash, UCB Pharma, Dr Eamonn Reading, University of Southampton

MdtEF-TolC is an efflux pump from Escherichia and Shigella Gram-negative bacteria which forms part of the wider resistance-nodulation-cell division (RND) protein family. It is upregulated within acidic and anaerobic conditions, with previous studies characterising its importance in cell survival during prolonged anaerobic growth, as well as its contribution to multidrug resistance (MDR) in clinical isolates and biofilm maintenance. However, key questions regarding mechanistic details of substrate binding and transport remained elusive due to the absence of structural information. Here, we report cryo-EM structures at < 3.6 Å resolution for the wildtype MdtF transporter and a single point mutant (V610F), which elicits an altered MDR phenotype, bound to the substrate Rhodamine 6G. Critically, these structures were characterised within styrene maleic acid lipid particles (SMALPs), a membrane mimetic which maintains membrane proteins within their intrinsic lipid mix. This enabled us to maintain proper transmembrane interactions and resolve lipids localised to the transmembrane region. With supporting biophysical characterisation, molecular modelling, and bacterial efflux and antimicrobial susceptibility assays we provide the foundational molecular insights into MdtF-mediated drug efflux and bacterial detoxification within acidic and anaerobic conditions.

10-Minute Talk: Is the mining of sequencing datasets for microbiota worthwhile? A case study reviewing Endometrial RNA-seq.

Richard Stack, University of Kent, Dr Gary Robinson, University of Kent, Dr Peter Ellis, University of Kent, Prof Sheryl Homa, Andrology Solutions, Dr Jane Cleal, University of Southampton.

The principal question in microbiome research is whether it is possible to accurately characterize the organisms that populate a specific habitat. The sensitivity and power of high-throughput sequencing creates multiple opportunities for bias, and this is especially true in the context of low microbial biomass. Some biological niches proposed to harbour distinct microbial communities, such as the placenta, have been refuted, highlighting the importance of establishing a biological signal distinct from contaminant nucleic acid. In addition, differences in the binding efficiencies of "universal" 16S amplicon primers results in altered taxa detection rates, creating challenges in measuring differential abundance in composite samples.

Here we consider RNA seq as an alternative method to characterize microbiota, and use this case study of Endometrial data to illustrate the pitfalls involved in studying a low biomass niche.

Sponsor Stall Schedule

Sponsor	Days Attending
Avantor Sciences	24 & 25 April
Azenta/GenWiz	24 & 25 April
BGI Genomics	24-April
Clinisciences	24-April
Haier Biomedical	24 & 25 April
LabLogic	24 & 25 April
Novogene	24-April
Promega	24-April
Proteintech	25-April
Proteintech	25-April
Thermofisher & Scientific Laboratory Supplies	24-April