# PICK 'N' MIX II

TIME: 15.25 – 16.05

LOCATION: DOBSON ROOM

## USING PRECISION CUT LUNG SLICES TO UNDERSTAND INNATE IMMUNITY DURING INFECTION AND INFLAMMATION

**Jacob Rudman, Sheffield Medical School, University of Sheffield**

Cryptococcus neoformans is an opportunistic fungal pathogen found worldwide. Despite diagnostic improvements, mortality rates remain as high as 80%. Cryptococcal infection in immunocompetent individuals is subclinical, meaning there is limited clinical data describing the 'ideal' immune response – limiting the development of new treatments. Research therefore relies on animal models, although current approaches lack mammalian immunity or aren't compatible with high-content imaging. We have developed an *ex vivo* murine precision cut lung slice (PCLS) model to visualise host-pathogen interactions in lung tissue.

8-13 week old C57BL/6 mice were sacrificed or 24 hours after intranasal GFP Cryptococcus neoformans inoculation. Lungs were perfused with 37oC agarose and cooled. 300µm lung slices were prepared and imaged by confocal or widefield microscopy. Isolectin IB4 GS or cell surface markers (CD11c, CD172α, CD88) identified innate leukocytes.

Slices are viable for >3 days and show preserved vasculature and alveoli. Instilled cryptococci replication *ex vivo* and *in vivo* were identical. Yeast cell size increases and intracellular survival was also preserved. Macrophages, not neutrophils or dendritic cells, significantly responded to cryptococcal infection. Phagocytosis only occurred 24 hours post infection. When infected with avirulent plb1-/- Cryptococcus, we observed significantly larger yeast cells that weren't phagocytosed by macrophages - suggesting phagocytosis is detrimental to the host. Additionally, we have investigated neutrophil microvesicles in COPD.

We have shown PCLS is a powerful technique for visualising immune responses in infection and inflammation. We now will manipulate this system pharmacologically and genetically to delineate the events required for cryptococcal clearance or dissemination.

## OPTIMISATION OF MESENCHYMAL STEM CELL CULTURE CONDITIONS FOR METABOLOMICS

**Zain Ghanameh, Institute of Ageing and Chronic Disease, University of Liverpool**

Metabolism instability may contribute to many diseases, including but not limited to cancer, obesity, cardiovascular diseases and diabetes. Not only do mesenchymal stem cells have high therapeutic potential, they also offer a powerful model for studying the metabolism of the maturation of certain differentiated cells, such as cardiomyocytes. Cardiomyocytes go through significant metabolic changes throughout their differentiation and maturation, the most significant change is the transition from anaerobic to oxidative metabolism. There is a switch in the metabolic profile of 'immature' glycolysis-dependent cardiomyocytes to mature cardiomyocytes, which predominately relies on oxidative metabolism. This switch is a key component for cardiomyocyte maturation. After birth, half of the ATP is produced via glycolysis in cardiomyocytes, after seven days, glycolysis decreases, accounting for less than 10% of ATP production. These changes couple with mitochondrial reorganisations to produce more efficient power beating cardiomyocytes, causing an increase in the number of mitochondria in each cell as a cardiomyocyte matures. Understanding the maturational mechanisms and their

contribution to changes in metabolic profile is essential as it may yield important insight into entry points in the control of cardiomyocyte maturation. A high-throughput proton (1H) nuclear magnetic resonance (NMR) metabolomics approach was introduced for systemic metabolic phenotype characterisation offering high analytical reproducibility and quantitative data. To study the effect of certain culture conditions on the metabolism of bone-marrow derived mesenchymal stem cells (BM-MSCs), sample preparations involve snap freezing BM-MSCs with liquid nitrogen for NMR acquisition followed by data analysis using Topspin, MetaboAnalyst, and Chenomx.

## VIEWS OF SPEECH AND LANGUAGE THERAPISTS ON ALTERNATIVE AND AUGMENTATIVE COMMUNICATION FOR CHILDREN WITH NEURODISABILITIES IN KUWAIT

**Nour Alreshaidan, Institute of Health and Society, Newcastle University**

Severe communication difficulties are common among children with neurodisabilities. Speech and Language Therapists (SLTs) provide services to facilitate communication development for children with neurodisabilities who have severe communication difficulties in collaboration with parents, carers and other health professionals, in a team approach. This can include introducing augmentative and alternative communication (AAC) systems, such as sign, communication boards, speech-generating devices, and mobile communication applications to supplement children's natural communication. At present AAC is seldom prescribed in Kuwait, although the reason for this is not known. This study aimed to understand the views of SLTs in Kuwait regarding the use of AAC, which may impact on the use and implementation of AAC systems.

Semi-structured interviews were conducted with nine SLTs in Kuwait working in governmental and private clinics, hospitals, and preschools to investigate their perspectives about the use of AAC, difficulties of communicating with children with severe communication problems, family and nanny involvement, and strategies used to facilitate communication. The interviews were recorded, transcribed *verbatim* and analysed thematically to create thematic networks. The research is in progress. This presentation will discuss preliminary facilitators and barriers of AAC implementation into practice identified by local SLTs working with children with neurodisabilities in Kuwait.

## WEARABLES AS OBJECTIVE TOOLS IN SPORT-RELATED CONCUSSION: A PROTOCOL FOR MORE INFORMED PLAYER MANAGEMENT

**Dylan Powell, Department of Computer and Information Sciences, Northumbria University**

Background: The prevalence of concussion in rugby is growing, but methods to support improved player welfare are lacking. Currently pitch-side return-to-play decisions are based on brief post-injury subjective observations, which may miss subtle effects that objective assessments can detect. The development of objective-tools to continuously monitor player welfare during this time is therefore of critical importance. The primary purpose of this project is to test the utility of wearable technology to monitor free-living/habitual gait as a potential clinical marker for concussion.

Methods: University-level rugby players (50M:50F) will be assessed over three seasons (2019-2022). All players will undergo pre-season testing including detailed medical history as well as a battery of clinical, cognitive, physiological (e.g. neck strength), motor (e.g. balance) tests. During each season, players suspected of concussion (training or matches) will be clinically examined by a physiotherapist and referred to the study. Examinations conducted at the baseline will be repeated immediately post-concussion (pitch-side and 24-hours), within the acute phase (7-14 days) and post-season for longitudinal assessment. Pitch-side gait and balance will be assessed using a discrete wearable with validated algorithms for data analysis. Between groups (concussed or non-

concussed) differences will be analysed with covariance for pre/post-season, and linear mixed models deployed to further examine concussed players at various time-points.

Conclusion: This project will determine the effectiveness of using wearable derived gait and balance data gathered during free-living as an objective method to better inform return-to-play protocols for players who suffer concussion. Thereby improving overall player welfare and safety in contact sports.