Names (Presenter in bold font)	**Alison K Carlisle**, Jürgen Götz, Liviu-Gabriel Bodea
Affiliations	Clem Jones Centre for Ageing Dementia Research, QBI
Title	Fibril amyloid-β decreases *de novo* protein synthesis in microglia *in vitro*
Abstract (max 300w)	Alzheimer's disease (AD) is a highly complex and fatal neurodegenerative disease for which there is no cure. It has been increasingly recognised that microglia, the brain's resident immune cells, play a crucial role in the progression of this disease. However, the details of this role are not fully understood. In AD, microglia cluster around extracellular aggregations of the peptide amyloid-β (Aβ), one of the main pathological characteristics of this neurodegenerative disease. As professional phagocytes, microglial cells internalise Aβ in an attempt to clear it away and restore brain homeostasis. The specific cellular mechanisms altered by Aβ internalisation, however, are yet to be fully elucidated. We are addressing this gap in knowledge by investigating de novo protein synthesis in microglia, hypothesising that the internalisation of Aβ by these cells would elicit specific alterations in cellular physiology that would be encapsulated in the de novo proteome. Using biorthogonal labelling and click chemistry techniques to tag, visualise and quantify these newly synthesised proteins, we show that internalisation of Aβ results in a fast decrease in protein synthesis in microglia in vitro. Furthermore, we reveal that this reduction is likely due to an activation of the integrated stress response (ISR), an evolutionarily conserved signalling pathway activated by various cellular stresses, including the presence of aggregated or misfolded proteins. Overall, our results provide novel insight not only into alterations of microglial function in AD, but also aspects of microglial physiology previously little explored. We next aim to validate these results in vivo and investigate if pharmacological inhibition of the ISR leads to an amelioration of the AD phenotype.

Abstract deadline: Jan 20 (Please send to cjcadradmin@qbi.uq.edu.au)