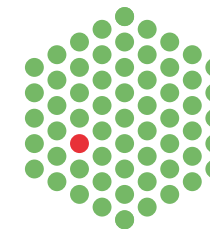


EMBL  
Australia



## Partner Laboratory Group Leader Applicant

### Mathew Blurton-Jones – 11:50am

*Department of Neurobiology and Behavior, Institute for Memory Impairments and Neurological Disorders  
University of California, Irvine*

#### Using Stem Cells to Treat and Model Alzheimer Disease

Age-related neurodegenerative disease represents one of the major challenges in modern biomedical research. The prevalence of disorders such as Alzheimer disease (AD) is expanding rapidly as our population ages, and current treatments have little or no effect on the pathways that underlie the neuropathology and cognitive dysfunction. The potential of regenerative medicine and stem cell biology to uncover novel and effective approaches to treat neurodegeneration has led to a renewed sense of optimism. However, a great deal of study is needed to determine whether stem cells can provide a useful approach to either treat or model AD. Recently, we showed that neural stem cells transplanted into the hippocampus of Alzheimer transgenic mice can rescue spatial learning and memory deficits despite widespread and established A $\beta$  plaque and neurofibrillary tangle pathology. Interestingly, cognitive function is improved without altering A $\beta$  or tau pathology. Instead, the mechanism underlying improved cognition involves a robust enhancement of hippocampal synaptic plasticity, mediated by brain-derived neurotrophic factor (BDNF). Both gain-of-function and loss-of-function studies have revealed that NSC-derived BDNF is critical to these effects. To follow up on these studies, we have begun to examine whether this approach can translated and enhanced for future clinical testing.

In parallel to these studies, we have also begun to examine whether human embryonic stem cells (ESCs) or induced pluripotent stem cells (iPSCs) can be used to model neurodegenerative disease *in vitro*. AD is a human-specific brain disorder and thus best modeled using human neurons. ES and iPS cells therefore offer a unique advantage in that they can be expanded and differentiated into mature physiologically functional neurons. To begin to examine the use of pluripotent stem cells to model AD, we have established novel human ES lines that produce elevated amounts of A $\beta$ , providing a valuable tool to identify drugs and genetic modifiers that regulate A $\beta$  production and degradation in human neurons. Interestingly, during the course of these studies, we have also uncovered a remarkable effect of amyloid precursor protein (APP) on ES cell differentiation. Examination of the underlying mechanism has revealed that a secreted soluble fragment derived from APP drives rapid and robust neural differentiation of human ES cells. Taken together, our findings demonstrate that stem cells can provide a powerful and promising approach to not only treat AD but to also model and examine the molecular and cellular basis of this devastating disease.

Wednesday

4 August

11:50am

Meeting Room G19

Ground Floor

STRIP (Building 75)

Monash University

Clayton