Names (Presenter in bold font)	**Heledd Brown-Wright**, Lidia Madrid San Martin, Leon Luan, Leszek Lisowski, Marco Morsch, Adam Walker.
Affiliations	The University of Queensland
Title	The University of Queensland, Macquarie University and Children's Medical Research Institute
Abstract (max 300w)	Accumulation of aggregated cytoplasmic TAR DNA binding protein 43 (TDP-43) is the pathological hallmark of amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND) and frontotemporal dementia. These neurodegenerative diseases are poorly treated, and therapeutically targeting aberrant TDP-43 protein is challenging since both increased and decreased TDP-43 levels are toxic. The biological processes of neurodegeneration caused by TDP-43 dysfunction remain poorly defined, and there is a lack of valid animal models mimicking the diversity of TDP-43 pathologies. We therefore aimed to develop new animal models with pathological TDP-43 expression, using viral delivery in mice. Adeno-associated viruses were used to express either EGFP control or wildtype TDP-43, cytoplasm-targeted TDP-43, or pathology-mimicking TDP-43 variants in non-transgenic C57BL/6J neonates delivered intracerebroventricularly at postnatal day 0. DNA constructs were packaged into the AAV9 type capsid and expression driven by the human synapsin promoter, for neuronal-specific expression. Mice were neurologically scored and underwent a battery or behavioural testing including activity monitoring, rotarod, and grip-strength testing for up to 12 months. Biochemical analysis indicated dramatic accumulation of detergent-insoluble and phosphorylated TDP-43 in pathology-mimicking TDP-43-expressing mice, and a subset of mice demonstrated behavioural phenotypes reminiscent of previously reported ALS mouse models. Viral-mediated TDP-43 mouse models may therefore represent valuable systems for investigation of the biological mechanisms of disease, with the added benefit of allowing rapid production of comparable cohorts of mice amenable to preclinical testing for ALS and FTD.

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