

P027 Phenotypic characterisation of CHMP2B knockout mice
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C-terminal truncating mutations in CHMP2B are a rare cause of frontotemporal dementia but the function of CHMP2B in the nervous system is presently unknown. We have generated CHMP2B knockout mice to gain insight into the normal function of CHMP2B and to determine whether loss of function of CHMP2B contributes to frontotemporal dementia caused by CHMP2B mutations. We used heterozygous embryos from BayGenomics in which the CHMP2B gene is disrupted by insertion of a gene trap vector into intron 2 for the generation of homozygous CHMP2B knockout mice. We used the modified SHIRPA protocol to systematically assess behaviour in mice at 12 months of age. To date we have found that CHMP2B knockout mice exhibit an adult onset phenotype including impaired righting reflex, an abnormal splayed gait and an abnormal posture in the front paws. Survival analysis using a Kaplan-Meier plot shows that homozygous CHMP2B knockout mice have a significantly reduced life span. These results suggest that loss of CHMP2B can have detrimental effects and further investigation is required to determine the pathological basis of these effects and their potential relevance to frontotemporal dementia caused by CHMP2B mutations.