Data input form: MouseAGE Database

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Preferred acknowledgement:

Summarise supporting data attached:

Tg6799 (5XFAD) is an Alzheimer's transgenic mice commercially available (MMRRC stock #34840). The model bears five familial mutations and develops an early heavy burden of brain amyloid with cognitive loss, inflammation and other AD traits. It is widely used in Alzheimer studies. It was created by R Vassar's group (Oakley et al., 2005).

Information and selected references are included.

Ageing / disease: Alzheimer

Model: Tg6799 (5XFAD)

Clinically relevant? (Yes or No): Yes

Explanation of why clinically relevant or not:

Mice bear three mutations of amyloid precursor protein (APP K670N/ M671L (Swedish), I716V (Florida), and V717 (London)) and two mutations of presenilin 1 (PS1 M146 and L286V) that promote rapid, aggressive and complete development of AD-like phenotype. Tg6799 is the 5XFAD line with higher amyloid burden as show in the original paper (Oakley et al., 2005).

Characteristics, timing of appearance of phenotype and phenotypic tests used (attach supporting data when unpublished if available):

There is a progressive increase in the AD-like pathology, with significant increase of amyloid levels and visible deposits at 3-4 months old. However, visible pathology starts in the cerebral cortex and full hippocampus affectation appears later at 5-6 months of age. Mice show significant neuroinflammation. Hyperphosphorylated tau is detected in the vicinity of plaques, with generally low tau pathology. Mild neuronal death in some specific areas was reported by several authors, but it is not easily detected. More publicactions are appearing and confirm the suitability for

experimental studies. Regarding behavioural testing, Tg6799 mice are hyperactive and may show increased variability in some tests. However, cognitive loss can be detected as early as 2 months, whereas responses of behavioural and psychological symptoms of dementia (BPSD)-like behaviour such as anxiety and lower exploration appear at late ages of 8 months. Spontaneous death of some animals appears after 10-12 months of age.

See references below for studies of characterization of cognitive and non-cognitive behaviour, amyloid pathology, tau, oxidative stress, inflammation and epigenetic changes (Rojas et al., 2013; Griñán-Ferré et al., 2016; Colié et al., 2017).

If applicable, Intervention(s) performed (type, dose, route of administration, frequency):

Interventions can be performed for studying neuroprotection.

Phenotype post-treatment (include null or negative results and attach supporting data separately):

Cognition may be recovered and pathology decreased by experimental treatments.

References (list below):

Strain

Oakley H, Cole SL, Logan S, Maus E, Shao P, Craft J, Guillozet-Bongaarts A, Ohno M, Disterhoft J, Van Eldik L, Berry R, Vassar R. Intraneuronal beta-amyloid aggregates, neurodegeneration, and neuron loss in transgenic mice with five familial Alzheimer's disease mutations: potential factors in amyloid plaque formation. J Neurosci. 2006;26(40):10129-40. PMID: 17021169

Studies

Colié S, Sarroca S, Palenzuela R, Garcia I, Matheu A, Corpas R, Dotti CG, Esteban JA, Sanfeliu C, Nebreda AR. Neuronal p38α mediates synaptic and cognitive dysfunction in an Alzheimer's mouse model by controlling β-amyloid production. Sci Rep. 2017;7:45306. doi: 10.1038/srep45306. PMID: 28361984

Griñán-Ferré C, Sarroca S, Ivanova A, Puigoriol-Illamola D, Aguado F, Camins A, Sanfeliu C, Pallàs M. Epigenetic mechanisms underlying cognitive impairment and Alzheimer disease hallmarks in 5XFAD mice. Aging (Albany NY). 2016;8(4):664-84. doi: 10.18632/aging.100906. PMID: 27013617

Rojas S, Herance JR, Gispert JD, Abad S, Torrent E, Jiménez X, Pareto D, Perpiña U, Sarroca S, Rodríguez E, Ortega-Aznar A, Sanfeliu C. In vivo evaluation of amyloid deposition and brain glucose metabolism of 5XFAD mice using positron emission tomography. Neurobiol Aging. 2013;34(7):1790-8. doi: 10.1016/j.neurobiolaging.2012.12.027. PMID: 23402900