

5xFAD Transgenic Mouse Model

5xFAD (Familial Alzheimer Disease) mice bear five mutations, three in the APP695 gene [K670N/M671L (Swedish), I716V (Florida), V717I (London)] as well as two mutations in the presenilin 1 gene [M146L, L286V]. Transgene expression is driven by the neuron specific Thy-1 promoter.

- Severe plaque load in cortex and hippocampus at 9 months of age
- Highly increased insoluble A β 1-42 and insoluble A β 1-40 levels in cortex and hippocampus at 9 months of age
- Severe neuroinflammation (CD11b; GFAP) in cortex and hippocampus at the age of 9 months
- Spatial learning deficits in 7 month old mice (MWM)

Morris Water Maze

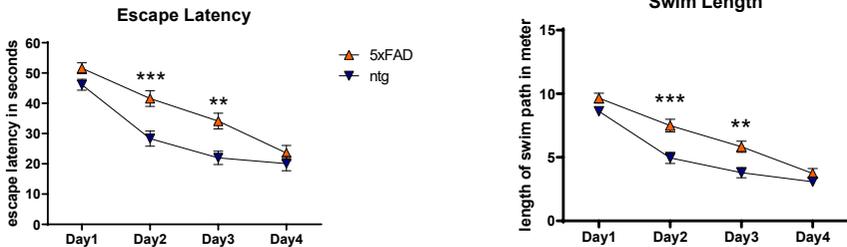


Figure 1. Morris water maze of 7 month old 5xFAD mice and non-transgenic (ntg) littermates. Mean \pm SEM; n = 12; Two-way ANOVA with Bonferroni's *post hoc* test; **p<0.01; ***p<0.001.

Neurofilament Light Chain

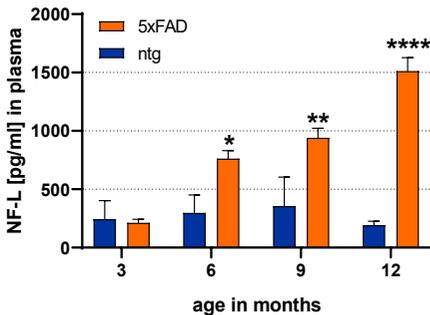


Figure 2. Neurofilament light chain in plasma of 5xFAD mice. NF-L levels in pg/ml in the plasma of 3, 6, 9 and 12 month old 5xFAD mice compared to non-transgenic littermates. Two-way ANOVA with Bonferroni's *post hoc* test. Mean + SEM. *p<0.05; **p<0.01; ****p<0.0001.

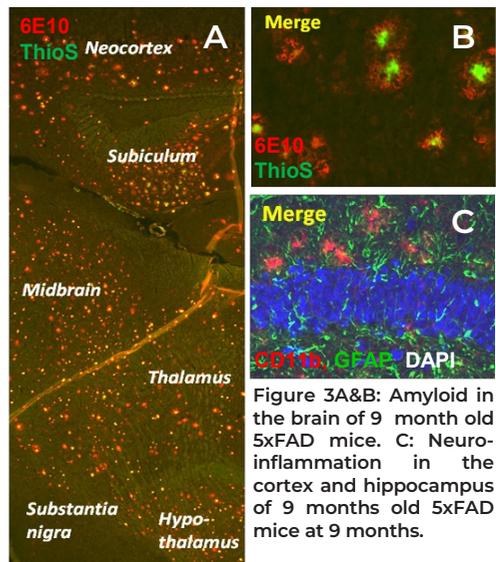


Figure 3A&B: Amyloid in the brain of 9 month old 5xFAD mice. C: Neuroinflammation in the cortex and hippocampus of 9 months old 5xFAD mice at 9 months.

Oakley et al. Intraneuronal β -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 Oct 4;26(40):10129-40.