

## Mouse Y-Maze Model for Cognition Enhancement in Alzheimer's Disease

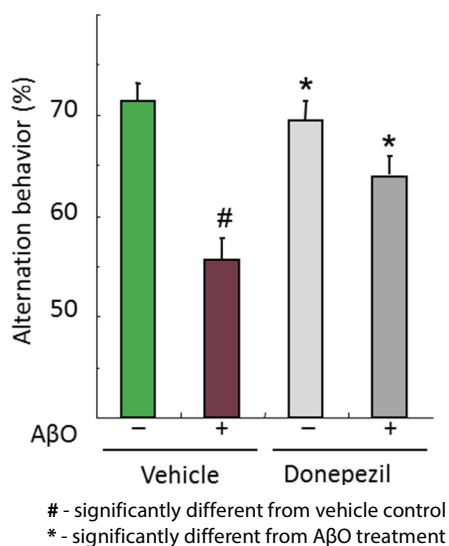
SynAging uses proprietary amyloid- $\beta$  oligomer (A $\beta$ O) preparations to induce Alzheimer's disease in mice following icv injection of 50 pmol. A $\beta$ O cognition impairment of the following amyloid peptides has been validated *in vivo*:

A $\beta_{1-42}$ , A $\beta_{1-40}$ , A $\beta_{11-40}$ , A $\beta_{11-42}$ , pE(3)A $\beta_{3-42}$ , pE(3)A $\beta_{3-40}$ , A $\beta_{4-40}$ , A $\beta_{4-42}$   
Others can be evaluated upon request.

SynAging's A $\beta$ O preparations induce full cognitive deficiency within four days, which remains stable over multiple months. SynAging has verified the cognitive deficiency of A $\beta$ O injected mice in the following assay formats:

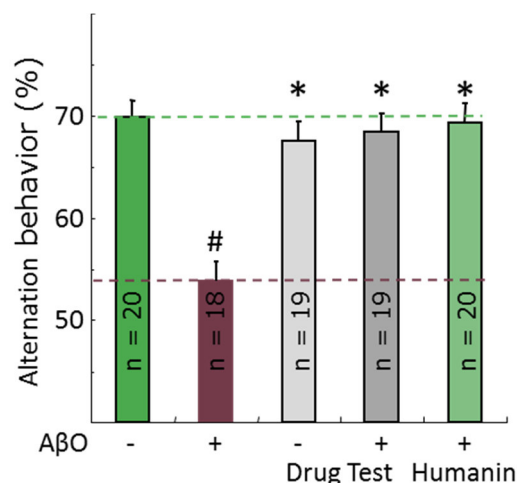
- Y-Maze (pre-frontal cortex)
- Novel Object Recognition (perirhinal cortex)
- Morris Water Maze (hippocampus)
- Spatial Recognition Test (hippocampus)

For evaluation of test compounds for dose-dependent cognition enhancement *in vivo*, we recommend the Y-maze assay: mice are icv injected with vehicle or 50 pmol A $\beta$ O (day 0) and test compound treatment started e.g. on day -1. The Y-maze model is performed on day 7, documenting symptomatic improvements during treatment.



Four days after icv injection of A $\beta$ O, alternation behavior in mice decreases significantly compared to vehicle injection. Donepezil (given po) can reverse this deficiency during treatment. Donepezil has no cognitive effect in icv vehicle injected mice.

**SynAging SAS:** Your partner in naturally induced phenotypic models, accelerating drug discovery for proteopathic CNS diseases



Cognitive improvement has been demonstrated using a test drug and humanin (positive control), both of which fully prevented the A $\beta$ O induced reduction in the natural alternation behavior.

**Timing:** results are available **one month** after study start incorporated in the draft report sent to clients. Final reports on test items, including client feedback, are provided two weeks later.

**SynAging's model shows very high reproducibility of A $\beta$ O induced cognitive decline.** Quality control has been performed over three year in 20 independent experiments using 11 batches of A $\beta_{1-42}$  oligomers. Mice were submitted to the Y-maze assay on day 4. While vehicle injected mice showed  $66.1 \pm 0.6\%$  alternation behavior, A $\beta$ O injected mice showed consistently reduced alternation at  $53.0 \pm 0.4\%$  (mean  $\pm$  SEM).

