SynAging Product Sheet 11

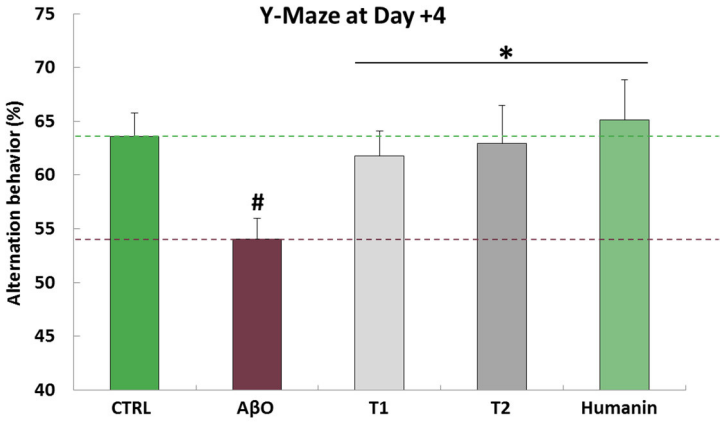
FAST Mouse Cognition Enhancement and Neuroprotection Assay for Alzheimer's Disease

SynAging uses proprietary amyloid-β oligomer (AβO) preparations to induce Alzheimer's disease in mice following icv injection of 50 pmol. AβO cognition impairment of the following amyloid peptides has been validated *in vivo*:
$Aβ_{1-42}$, $Aβ_{1-40}$, $Aβ_{11-40}$, $Aβ_{11-42}$, $pE(3)Aβ_{3-42}$, $pE(3)Aβ_{3-40}$, $Aβ_{4-40}$, $Aβ_{4-42}$
Others can be evaluated upon request.

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

- Y-Maze (pre-frontal cortex)
- Novel Object Recognition (perirhinal cortex9
- Morris Water Maze (hippocampus)
- Spatial Recognition Test (hippocampus)

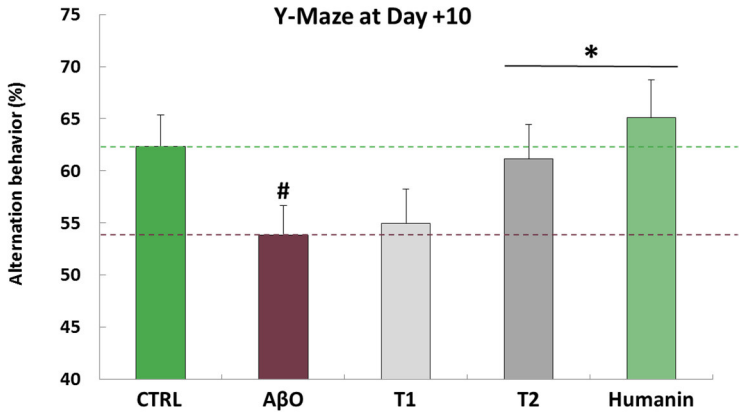
For a *FAST* evaluation of test compounds *in vivo*, we recommend the double-Y-maze model. In this, mice are icv injected with vehicle or AβO (day 0) and test compound treated from e.g. day -1 to day 7. The first Y-maze is performed on day 4, documenting symptomatic improvements during treatment.



- significantly different from CTRL, * - significantly different from AβO

Four days after icv injection of AβO, alternation behavior in mice is significantly decreased compared to vehicle injection. Compound T1 and T2 (both given po), as well as the positive control humanin (icv) prevent this deficiency.

Drug treatment is stopped on day seven and a second Y-maze assay is run on day ten investigating disease modifying properties.

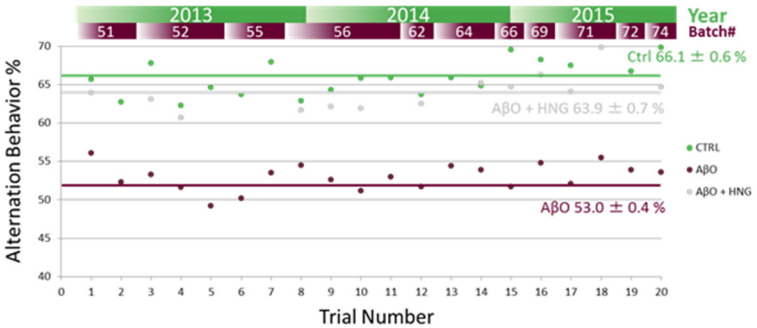


- significantly different from CTRL, * - significantly different from AβO

The deficiency in alternation behavior on day 10 in AβO mice without compound treatment is unchanged. Treatment with T1 had no lasting effect, whereas T2, as well as humanin treatment show clear disease modification.

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 AβO induced cognitive decline. Quality control has been performed over three year in 20 independent experiments using 11 batches of $Aβ_{1-42}$ oligomers. Mice were submitted to the Y-maze assay on day 4. While vehicle injected mice showed 66.1 ± 0.6 % alternation behavior, AβO injected mice showed consistently reduced alternation at 53.0 ± 0.4 % (mean ± SEM).



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

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