SynAging Product Sheet 14

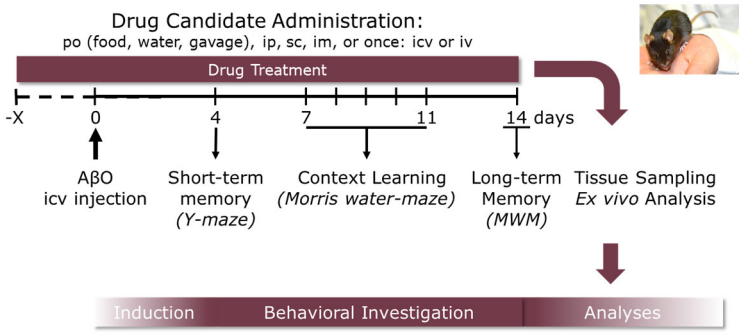
# Mouse Full Cognition Enhancement Assay in Alzheimer's Disease

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

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

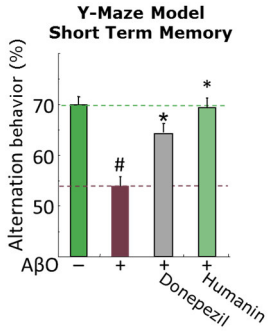
- Y-Maze (pre-frontal cortex)
- Novel Object Recognition (perirhinal cortex9
- Morris Water Maze (hippocampus)
- Spatial Recognition Test (hippocampus)

**Full evaluation of test compound-mediated cognition improvement in the Y-Maze and Morris Water Maze assays:** mice are injected icv with vehicle or AβO (day 0) and treated with drug candidates starting e.g. on day -1 for 15 days. The Y-Maze assay is performed on day 4, documenting short term memory improvements on drug candidate treatment.



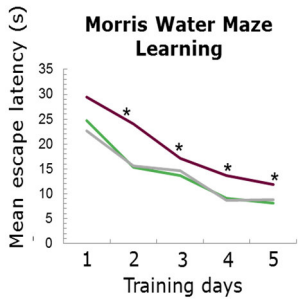

Context learning in the Morris Water Maze is performed on days 7 to 11 and the final long term memory readout is undertaken on day 14. Thereafter, plasma and brain can be collected for further analysis.

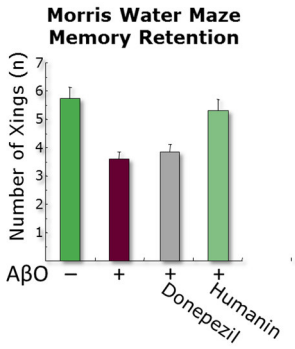
**The Y-Maze assay** of spontaneous alternation between different arms is strongly affected by AβO. Failure to perform in this assay indicates cortex deficits in short term memory. SynAging has shown a highly reproducible decline from 66.1 ± 0.6 % alternation in vehicle injected mice to 53.0 ± 0.4 % alternations in AβO injected mice in a quality control effort over three years.




Symptomatic compounds like Donepezil show a dose-related rescue in this model. 100 nM humanin (a human anti-apoptotic peptide: Yen, *et al.*, 2013, J. Mol.Endocrinol.; 50(1):R11-9) shows a full reversal of the AβO-induced cognitive decline.

**The Morris Water Maze assay** is testing spatial learning and long term memory retention, strongly involving hippocampal function. Mice are placed in a round water tank with optical clues on the walls for orientation and a platform submerged under water. The mice are released at various locations in the water and search for the hidden platform to escape onto it. Over multiple trials, mice learn the location of the platform. Mice that have been brain infused with AβO need more time to find the platform. Donepezil can improve learning.




Three days after the last training, the memory retention trial is performed. Mice are placed in the same basin, however, this time without the platform. For one minute the behavior is video monitored, the number of crossings over the former platform location is counted. Another readout is the time until the first crossing of the former platform location. Humanin, but not Donepezil, can restore long term memory in mice with AβO-induced cognitive decline.

**Timing:** study results are available within one month.

**SynAging will adapt the set-up to the requirements of your project.**

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