SynAging

Au coeur de la mémoire.

β-Amyloid Oligomer-Induced Alzheimer's Model Shows Synaptic Degradation for Use in Target Validation and Drug Development

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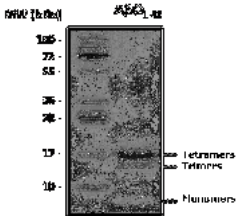
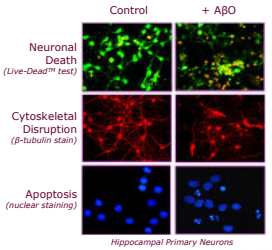
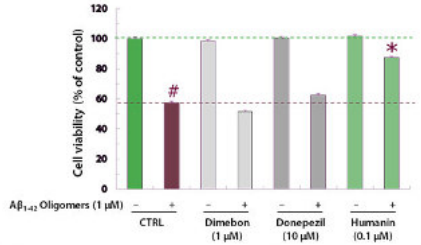
- Oligomeric forms of β-amyloid peptide (AβO) are widely accepted as the initial cause for neurodegeneration in Alzheimer's disease (AD)
- Translational *in vitro* and *in vivo* models are essential to reduce the significant attrition during drug discovery for neurodegenerative diseases
- Here, we report highly reproducible *in vitro* and *in vivo* AD models, induced by a single icv injection of SynAging's proprietary low-number AβO preparation
- AβO induce neuronal cell death in rodent primary neurons, as well as in iPS cell derived human neurons
- In rodent models (mice and rats), a single brain injection of minute amounts of AβO results in dramatic and fast impairment of cognitive functions fully established after one week and stable for months
- AβO-induced synaptic loss is shown
- AβO-induced release of pro-inflammatory cytokines is shown
- Unlike transgenic models, SynAging's models imitate sporadic AD

AβO Induced Neurotoxicity in rodent primary neurons

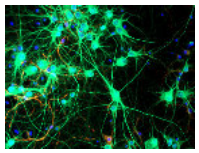


Aβ Species	Functional Effects		
	In vitro	*In vitro*	*In vivo*
	Oligomerization / Aggregation	Neurotoxicity	Cognitive deficits
Standard: $A\beta_{1-42}$	Yes	Yes	Yes
$A\beta_{1-43}$	Yes	Yes	Yes
$A\beta_{11-42}$	Yes	Yes	nd
$A\beta_{11-40}$	Yes	Yes	nd
$pE(3)A\beta_{3-42}$	Yes	Yes	Yes
$pE(3)A\beta_{3-40}$	Yes	n.d.	n.d.
$A\beta_{1-40}$	Yes	Yes	Yes
$A\beta_{3-42}$	Yes	Yes	Yes

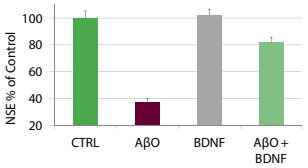




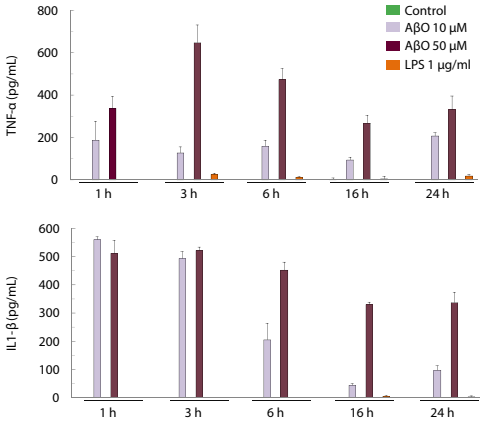
AβO-Induced degeneration on Human iPS Cell-Derived Neurons



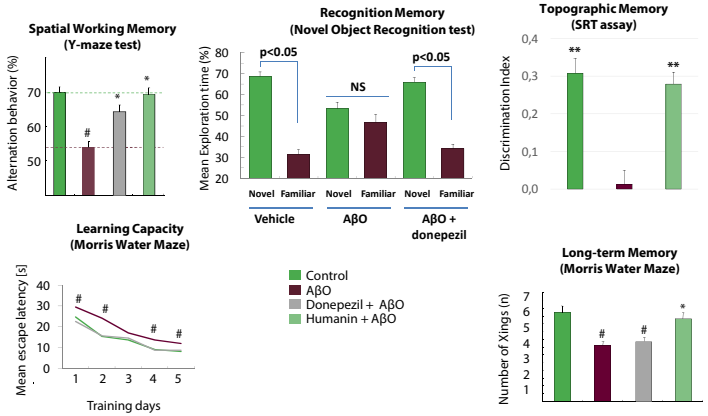
- HIP™ - Neurons derived from human IPS cells from MTI-GlobalStem cultured for five weeks
- Top: Cells fixed and labeled: MAP2 (green) neurons, GFAP (red) glia cells, and DAPI (blue) cell cores. Culture contains approximately 30 – 40 % neurons
- Bottom: AβO induced >60% neuronal loss, which can be recued by BDNF. Readout is neuron specific enolase (NSE) ELISA.



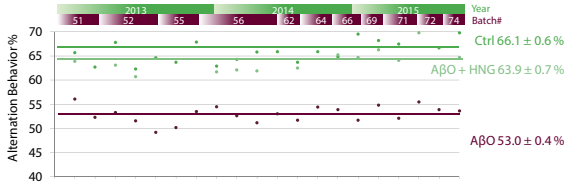
AβO Induce Pro-inflamatory Cytokine Release from Mouse Primary Astrocytes (ELISA measurements)



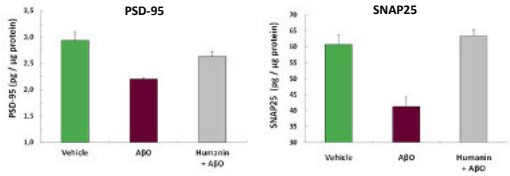
AβO-Induced Cognitive Decline and Synaptic Loss in Mice



sign. diff. from control; * sign. diff. from AβO, P < 0.5, ** sign. diff. from AβO, P < 0.1



Long term reproducibility of AβO induced cognitive decline in the Y-maze over three years and many batches of AβO



AβO induced decrease of hippocampal synaptic proteins (ELISA)