Selected opportunities in Neuroscience

Autophagy inducer TAT-Beclin reduces age-related cognitive decline (BIO17325)

AUTOPHAGY INDUCER TAT-BECLIN REDUCES AGE-RELATED COGNITIVE DECLINE (BIO 17325)

Product factsheet

In Vivo PoC

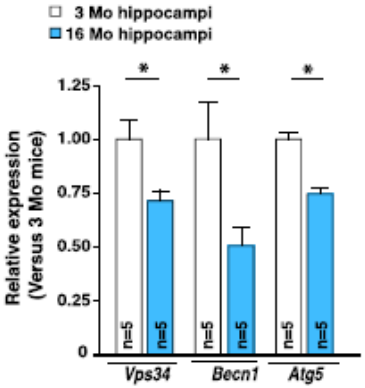
- **Target:**
  - Beclin / Autophagy
- **Product:**
  - TAT-Beclin peptide
- **Application:**
  - Age-related cognitive decline
- **Rational / POC:**
  - Hippocampus is essential for the regulation of memory functions, adult neurogenesis and is the main brain region affected by aging
  - The major autophagy genes related proteins are highly expressed in the hippocampus
  - Autophagy activity in the hippocampus decreases during aging / this decrease correlates with the decline of memory functions during aging
  - Autophagy-related markers are altered in in the hippocampus of old mice
  - Promoting autophagy in old hippocampi is sufficient to reverse age-Impaired memory
- **Patent and publication:**
  - Patent: “METHOD TO RESTORE OR IMPROVE COGNITIVE FUNCTIONS”. Priority: 04 October 2018
  - Publication: “Autophagy Is Required for Memory Formation and Reverses Age-Related Memory Decline”. Glatigny et al., Current Biology. Feb 2019.

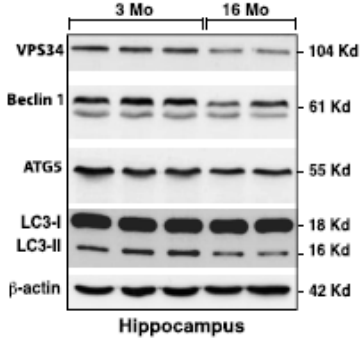
AUTOPHAGY INDUCER TAT-BECLIN REDUCES AGE-RELATED COGNITIVE DECLINE (BIO 17325)

Proof of concept

Autophagy-related markers are altered in the hippocampus of old mice

Reduction of autophagy-related genes in old mouse hippocampus

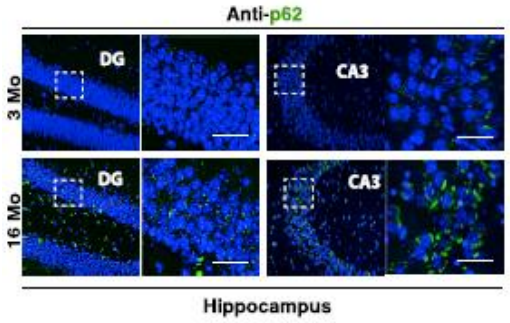


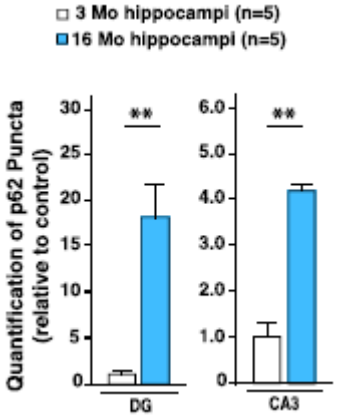


qRT-PCR and Western Blot experiments show a reduction of VPS34, Beclin 1 and ATG5 at the RNA (left) and protein (right) level in the hippocampus of old (16 months) compared to young (3 months) mice.
LC3-II accumulation is also decreased which further reflects a reduction in autophagy activity.

Increase of p62 accumulation in old mouse hippocampus

p62 immunostaining (left) and puncta quantification (right) performed on brain cross-sections, at the level of the hippocampal dentate gyrus (DG) and CA3 regions of 3 and 16-month-old mice . Quantification was performed relative to 3-month-old mice.
=> p62 accumulation reflects autophagy defect in old mice





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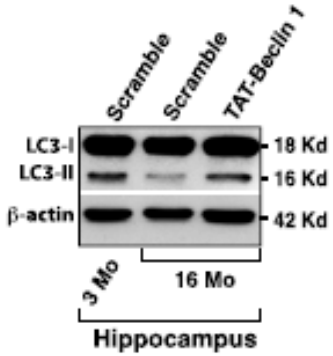
Proof of concept

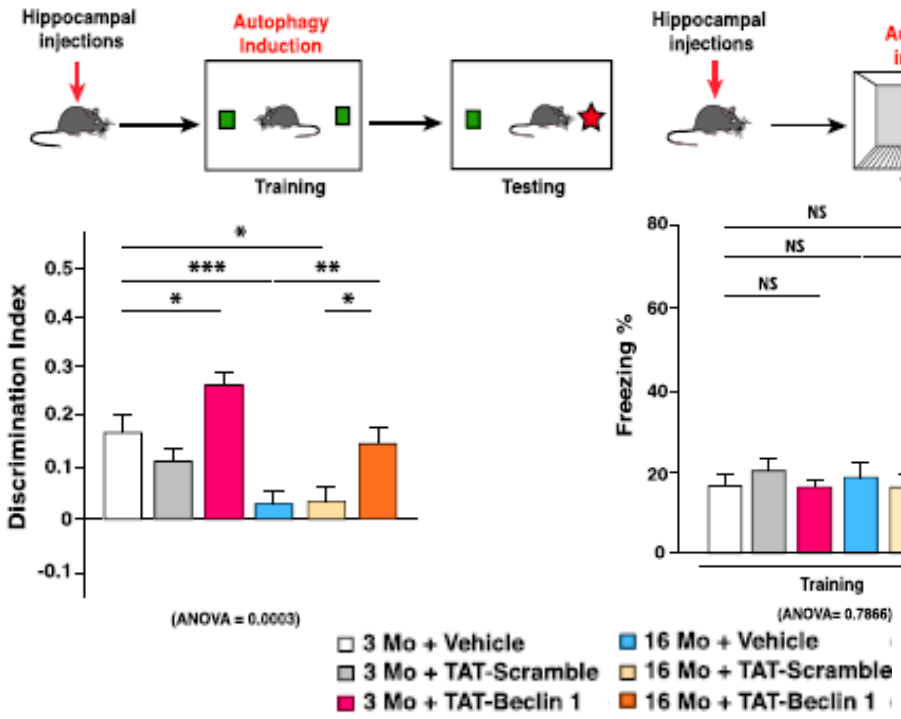
TAT-Beclin administration reverses age-Impaired memory

LC3 accumulation and memory are resored in old mice (16 months) injected with TAT-Beclin

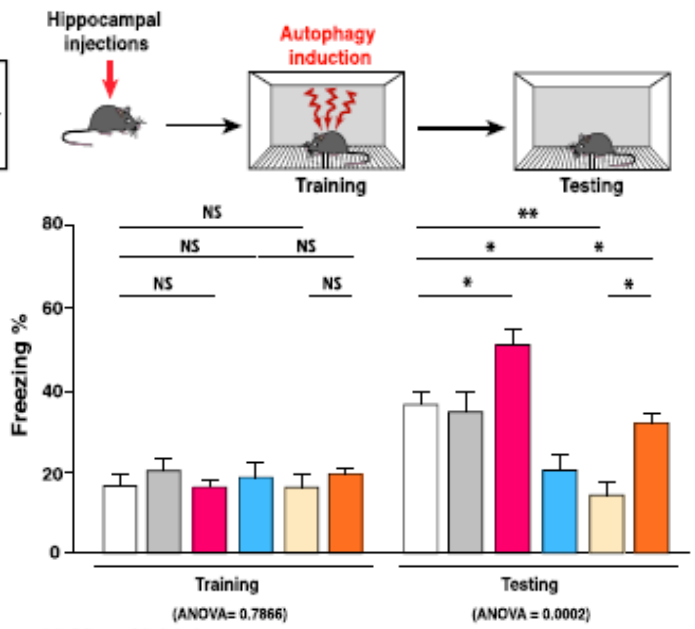
LC3-I and II accumulation

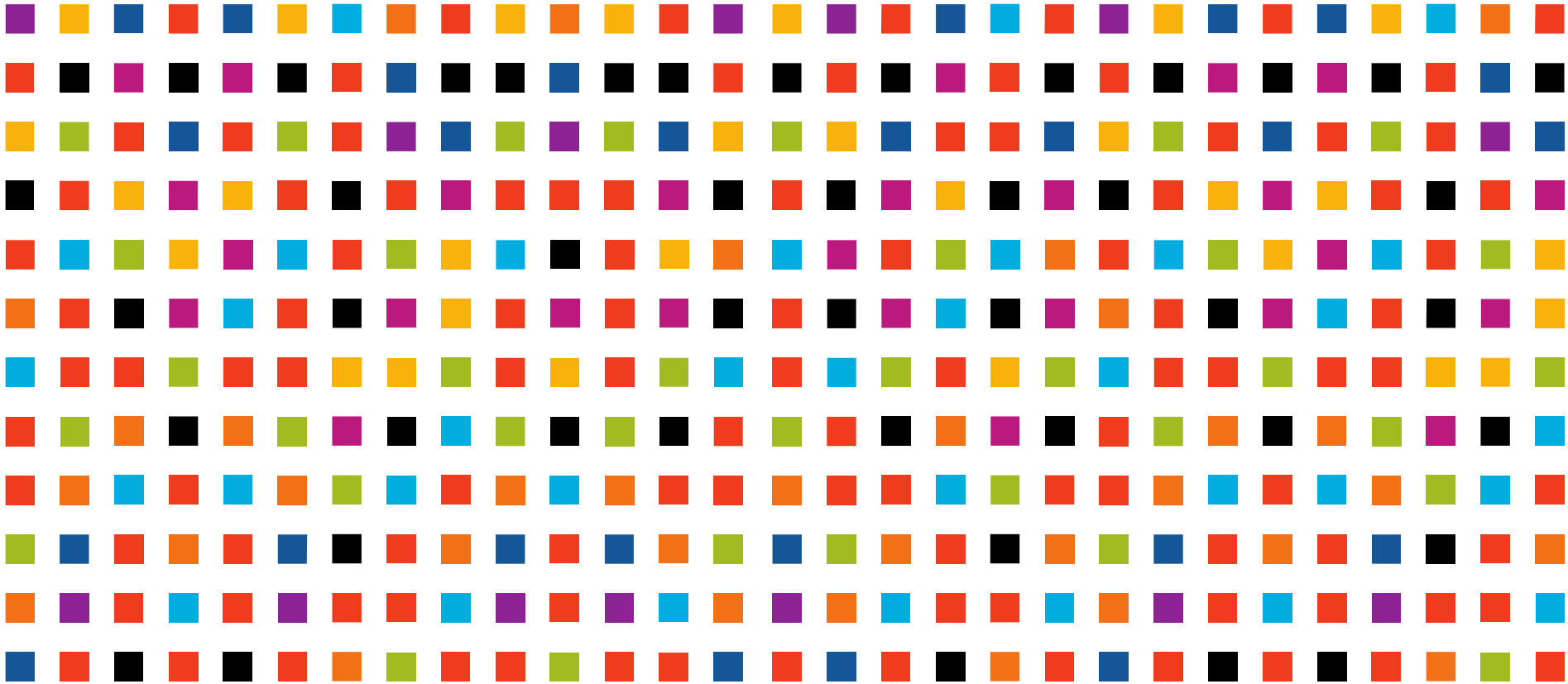


Novel object recognition test (NOR)



Contextual Fear Conditioning (CFC)





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