SELECTED OPPORTUNITIES IN NEUROSCIENCE

Pyk2-based gene therapy attenuates cognitive deficits associated to Alzheimer's Disease (BIO17059)

PYK2-BASED GENE THERAPY ATTENUATES COGNITIVE DEFICITS ASSOCIATED TO ALZHEIMER'S DISEASE (BIO 17059)

Product factsheet

In vivo PoC

- **Target:**
  - Pyk2
- **Product:**
  - Adeno associated virus expressing Pyk2
- **Application:**
  - Alzheimer's Disease
- **Technology:**
  - AAV-based gene therapy
- **Rational / POC:**
  - Pyk2 is a non-receptor calcium-dependent tyrosine kinase highly expressed in the hippocampus
  - *PTK2B,* the gene encoding Pyk2, is a susceptibility locus for Alzheimer's disease
  - Pyk2 knockout impairs hippocampal-dependent memory and LTP in mouse
  - NMDA receptors and PSD-95 are altered in Pyk2 mutant mice
  - Dendritic spines are altered in the hippocampus of Pyk2 mutant mice
  - Pyk2 phosphorylation (activation) and synaptic markers are altered in Alzheimer's disease (AD)
  - Pyk2 over expression through hippocampal AAV injection rescues memory in an AD mouse model
- **Patent and publication:**
  - Patent EP17305340 / Priority date 24 March 2017
  - Publication : "PTK2B/Pyk2 overexpression improves a mouse model of Alzheimer's disease". Giralt et al. Exp Neurol. 2018; 307:62-73.

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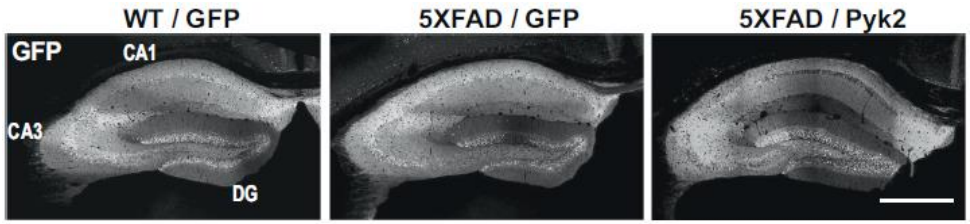
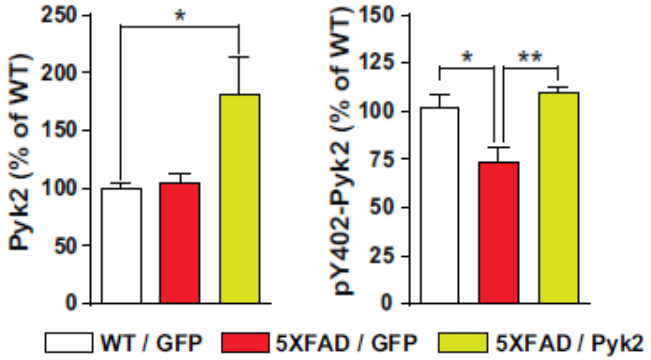
Proof of concept

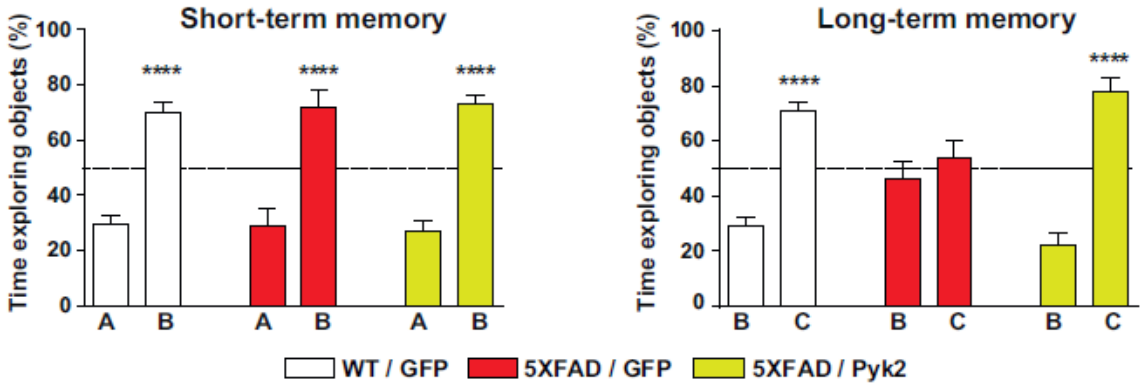
- **Pyk2 over-expression in the hippocampus of 5xFAD mice improves long-term memory**
  - AAV-mediated overexpression of Pyk2 in wt and 5xFAD mice



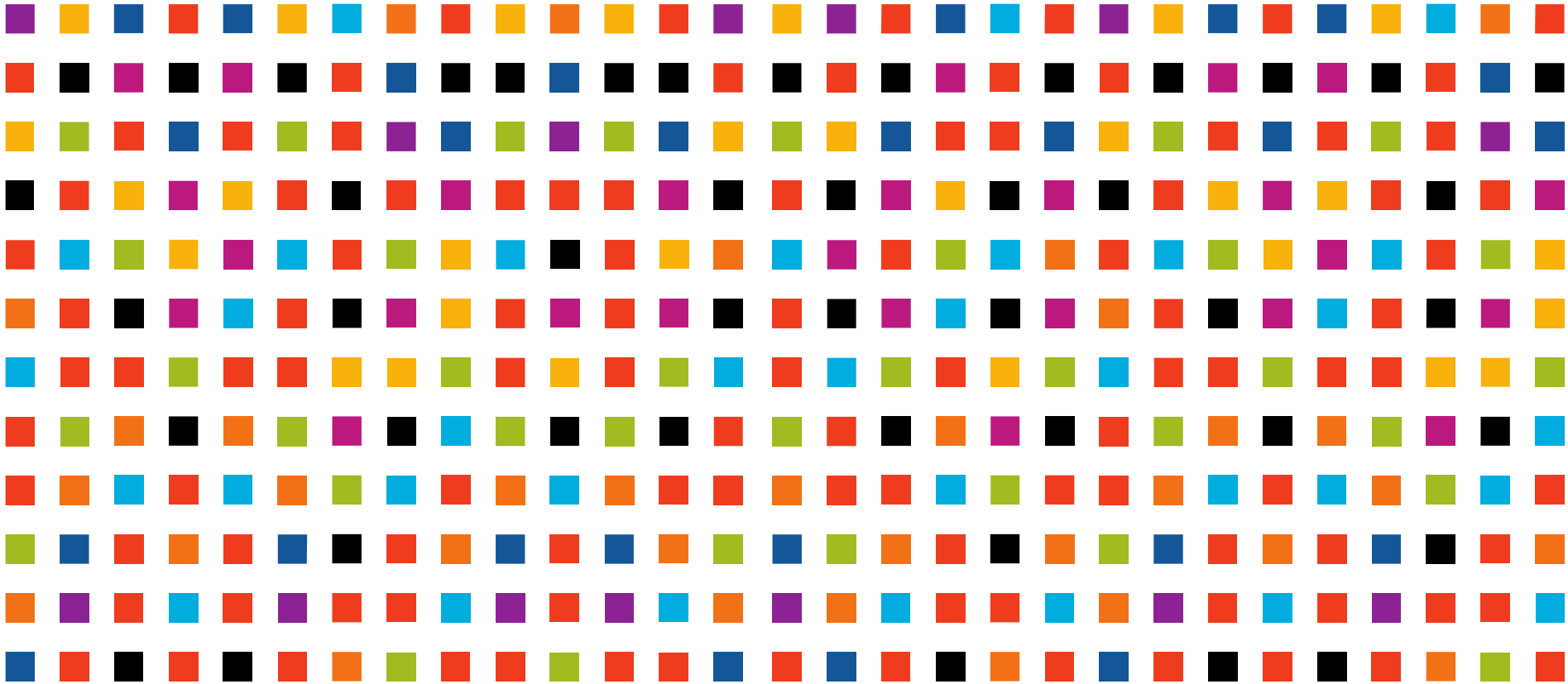
Wt and 5xFAD mice were bilaterally injected in the hippocampus with AAVs expressing ProtX or GFP. Quantification showed a restoration of protX phosphorylation level.



  - Pyk2 overexpression restores long-term memory in 5xFAD mice



Short-term memory (STM) was evaluated using the novel object recognition test. Long-term memory (LTM) was evaluated using the novel object recognition test 24 h after the STM trial.



ANNE.COCHI@INSERM-TRANSFERT.FR

Inserm Transfert - Paris Biopark
7 Rue Watt - 75013 Paris
Tel: +33 1 55 03 01 00 / Fax: +33 55 03 01 60
www.inserm-transfert.fr