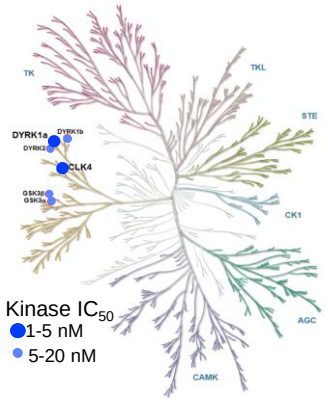
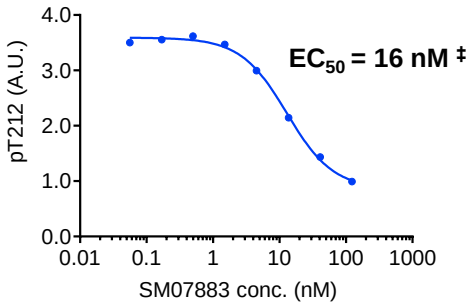
SM07883, a novel, oral DYRK1A kinase inhibitor, reduced tau pathology and associated behavioral deficits in preclinical models

Specifically inhibited DYRK1A and reduced pTau *in vitro*

Kinases within 15-fold of DYRK1A IC_{50}

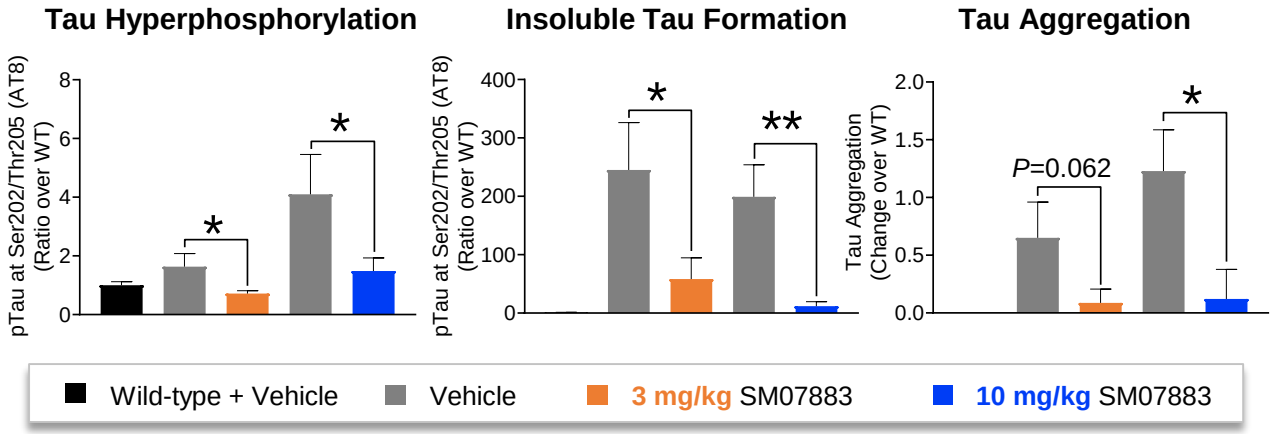


Tau pThr212
(HEK293)



‡Measured by immunoassays
Note: EC_{50} = average across multiple assays

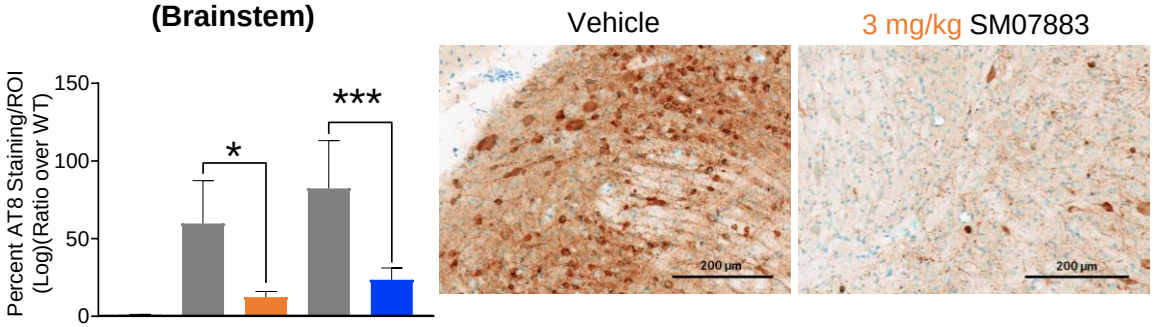
Inhibited tau pathology in JNPL3 mouse brains



Only 3 mg/kg normalized by β-actin

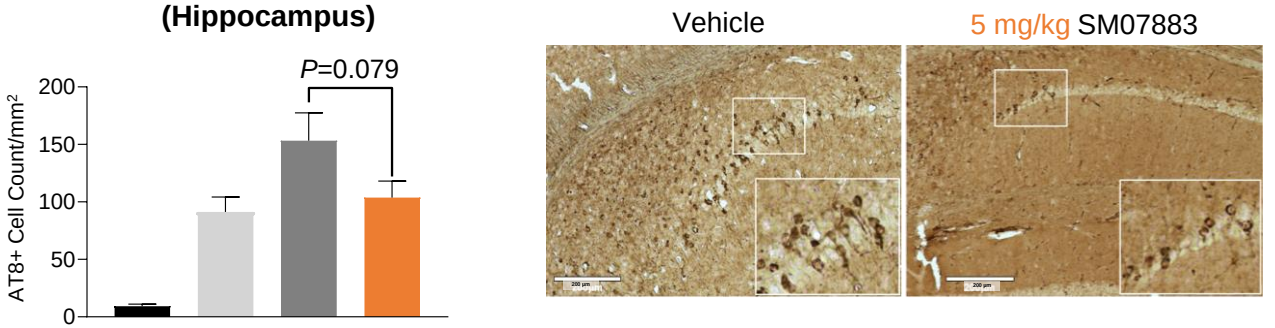
Inhibited tau pathology in JNPL3 mouse brains

Tau-positive Inclusions (Brainstem)



Inhibited tau pathology in 3xTg-AD mouse brains

Tau-positive Inclusions (Hippocampus)



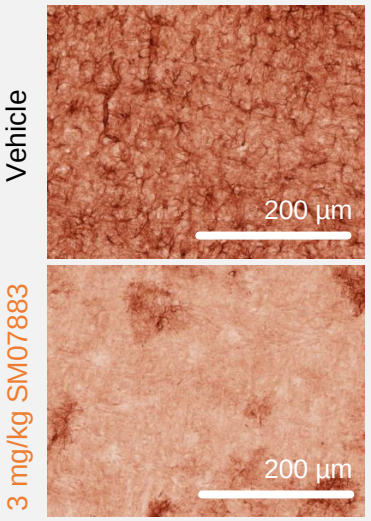
samumed

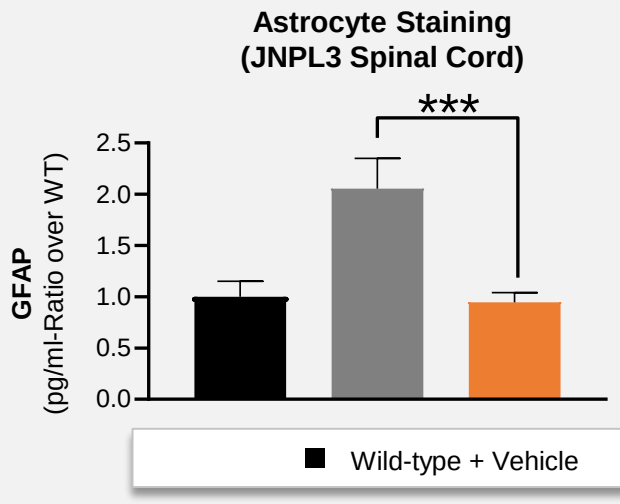
Melchior B, et al. *Aging Cell*. 2019.

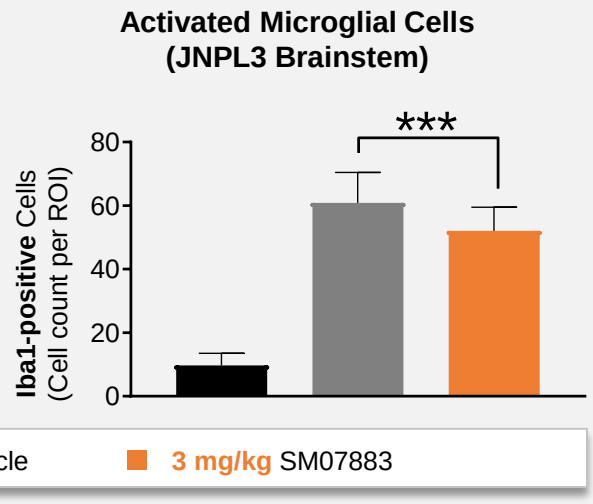
Mean ± SEM; **P*<0.05, ***P*<0.01, ****P*<0.001 vs. vehicle

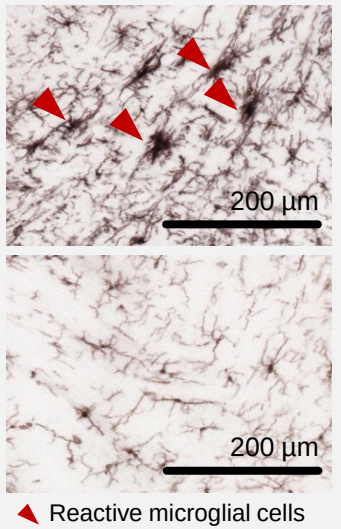
SM07883 reduced neurodegeneration-induced neuroinflammation in transgenic mouse models

JNPL3





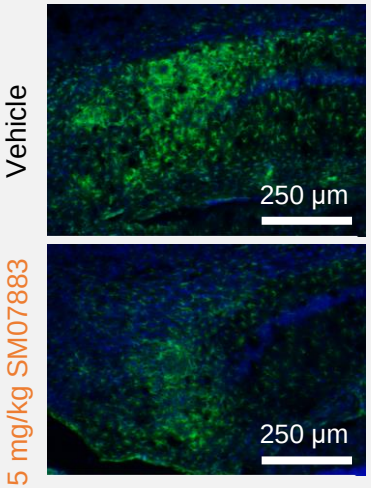


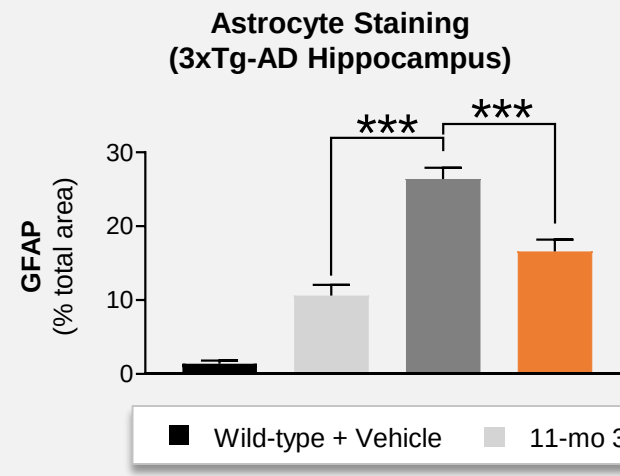


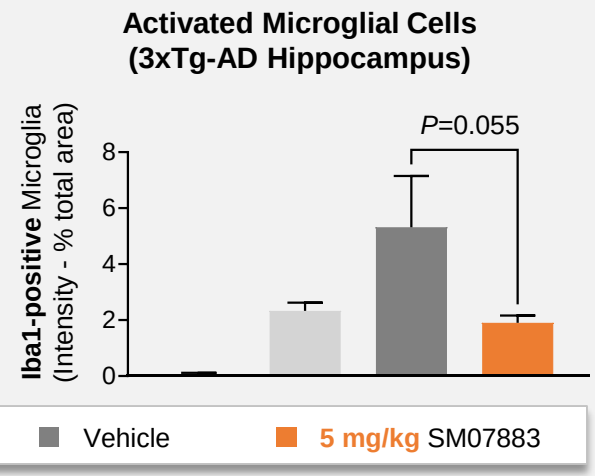
Wild-type + Vehicle | Vehicle | **3 mg/kg** SM07883

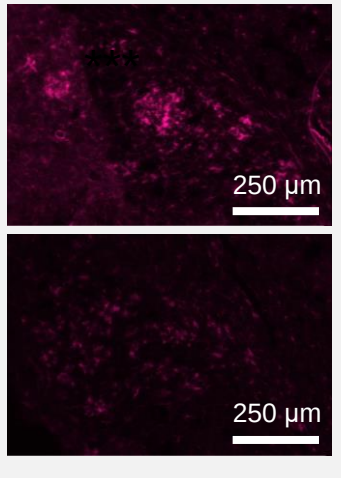
Reactive microglial cells

3xTg-AD









Wild-type + Vehicle | 11-mo 3xTg-AD | Vehicle | **5 mg/kg** SM07883

samumed

Melchior B, et al. *Aging Cell*. 2019.

Mean ± SEM; ***P<0.001 vs. vehicle

SM07883 significantly reduced functional and cognitive deficits in transgenic mouse models

JNPL3

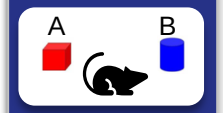
Wire Hang Test - Task Score
(Positive=improvement;
Negative=deterioration)

Vehicle

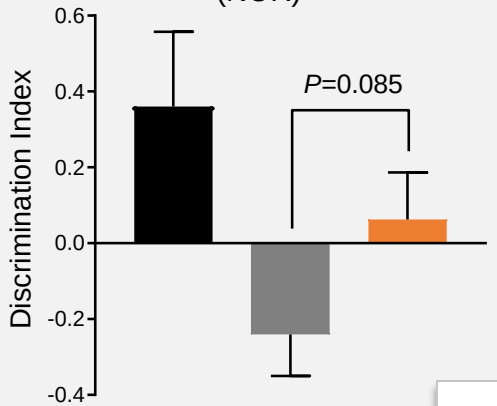
SM07883

Wild-type + Vehicle | Vehicle | **3 mg/kg/day** SM07883

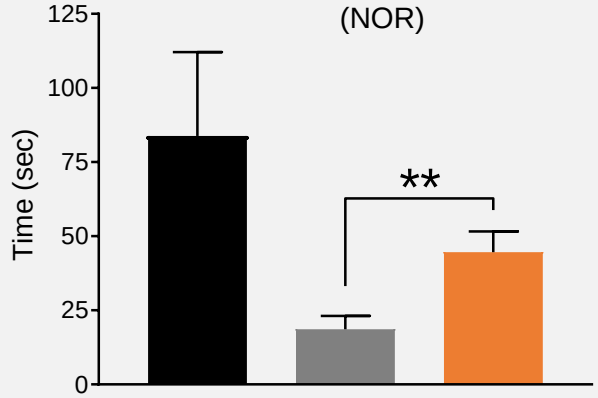
3xTg-AD



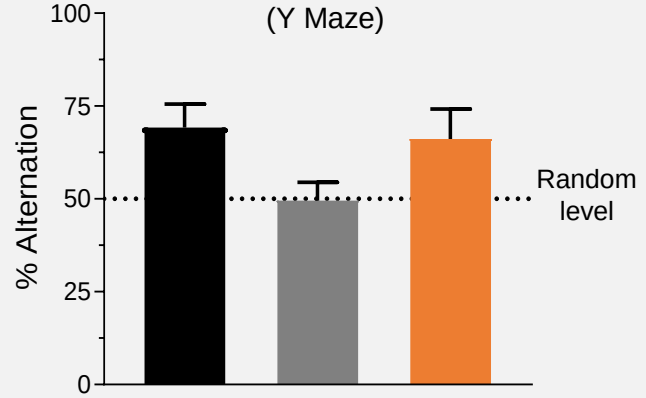
Discrimination Index
(NOR)



Time Spent Near Novel Object
(NOR)



Percent Alternation
(Y Maze)



Wild-type + Vehicle | Vehicle | **5 mg/kg/day** SM07883

samumed

Melchior B, et al. *Aging Cell*. 2019.

Mean ± SEM; **P*<0.05, ***P*<0.01 vs. vehicle