

A Neuronal Cell Line overexpressing Hyperphosphorylated Human Mutant TAU

Compound testing for the following indications:

- Alzheimer's Disease
- Parkinson's Disease
- Tauopathies

Model:

SH-SY5Y cells were stably transfected with human TAU441 harboring two disease related mutations (V337M/R406W). Transfected SHSY-5Y cells express human mutant TAU. Upon differentiation with retinoic acid, TAU protein levels were further elevated. Human TAU was shown to be hyperphosphorylated at multiple sites linked with AD (pThr181, pSer202, pThr231, and pSer396/Ser404). The Jun-Kinase (JNK) inhibitor SP600125 reduced Tau phosphorylation at various p-Tau epitopes including pThr231. This cell line allows to screen compounds targeting TAU protein and TAU phosphorylation.

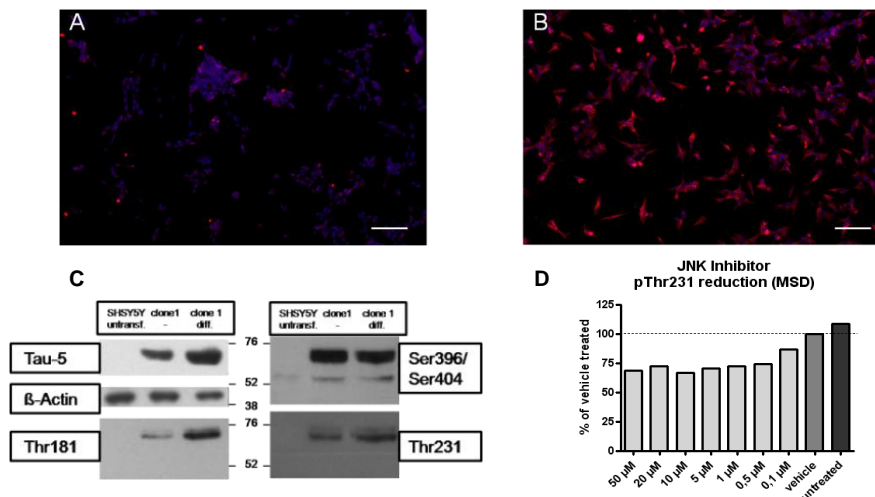


Fig.1. Immunocytochemistry showing overexpression of hTau441-V337M/R496W in (B) transfected and (A) in untransfected SHSY5Y cells (Scale bar 100µm). Human TAU is indicated in red, DAPI in blue. (C) Tau phosphorylation in undifferentiated and differentiated SHSY5Y-CMV-hTau441-V337M/R496W cells, and in control SHSY-5Y cells was examined by Western blot analysis. (D) pThr231 was reduced in SHSY5Y-CMV-hTau441-V337M/R496W cells in an immunosorbent assay (MSD) after treatment with the JNK inhibitor SP600125.

Endpoints:

Western blot: Total TAU, pThr231, pThr181, pSer396/pSer404

Immunosorbent Assay (MSD): Total TAU, pThr231

Mass Spectrometry: e.g. pThr231, pThr181, pSer396