Dexibuprofen prevents neurodegeneration and cognitive decline in APPswe/PS1dE9 through multiple signaling pathways

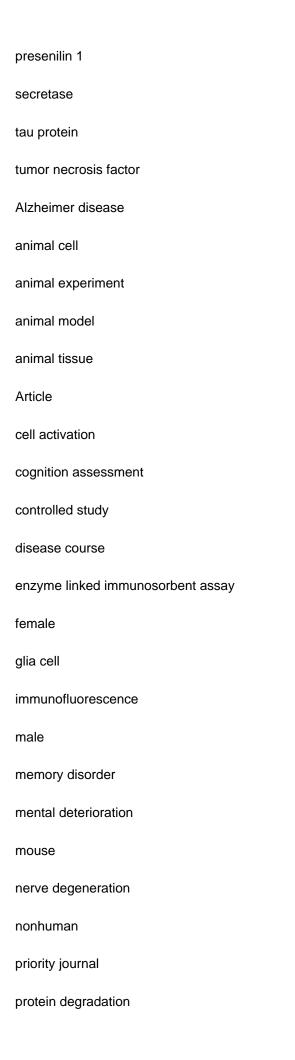
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The aim of the present study is to elucidate the neuronal pathways associated to NSAIDs causing a reduction of the risk and progression of Alzheimer's disease. The research was developed administering the active enantiomer of ibuprofen, dexibuprofen (DXI), in order to reduce associated gastric toxicity. DXI was administered from three to six-month-old female APPswe/PS1dE9 mice as a model of familial Alzheimer's disease. DXI treatment reduced the activation of glial cells and the cytokine release involved in the neurodegenerative process, especially TNF?. Moreover, DXI reduced soluble ?-amyloid (A?1-42) plaque deposition by decreasing APP, BACE1 and facilitating A? degradation by enhancing insulin-degrading enzyme. DXI also decreased TAU hyperphosphorylation inhibiting c-Abl/CABLES/p-CDK5 activation signal pathway and prevented spatial learning and memory impairment in transgenic mice. Therefore, chronic DXI treatment could constitute a potential AD-modifying drug, both restoring cognitive functions and reversing multiple brain neuropathological hallmarks. © 2017 The Authors

Alzheimer's disease

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APPSwe/PS1dE9
Dexibuprofen
Hippocampus
Insulin receptor
Memory impairment
Mitochondria
TAU
Abelson kinase
amyloid beta protein[1-42]
beta secretase 1
cyclin dependent kinase 5
dexibuprofen
tau protein
Abelson kinase
amyloid precursor protein
aspartic proteinase
Bace1 protein, mouse
Cables1 protein, mouse
carrier protein
Cdk5 protein, mouse
cyclin dependent kinase 5
cycline
dexibuprofen
ibuprofen
neuroprotective agent
phosphoprotein



protein phosphorylation
real time polymerase chain reaction
signal transduction
spatial learning
treatment outcome
treatment response
Western blotting
Alzheimer disease
analogs and derivatives
animal
brain
C57BL mouse
cognition
drug effects
genetics
metabolism
signal transduction
Alzheimer Disease
Amyloid beta-Protein Precursor
Amyloid Precursor Protein Secretases
Animals
Aspartic Acid Endopeptidases
Brain
Carrier Proteins
Cognition
Cyclin-Dependent Kinase 5

Cyclins
Female
Ibuprofen
Mice
Mice, Inbred C57BL
Neuroprotective Agents
Phosphoproteins
Presenilin-1
Proto-Oncogene Proteins c-abl
Signal Transduction
tau Proteins
Tumor Necrosis Factor-alpha