Allal Boutajangout et al., J Neurol Neurophysiol 2017, 8:6(Suppl)
DOI: 10.4172/2155-9562-C1-059

Inhibition of GSK-3β using ING-135 in an Alzheimer's disease mouse model

Allal Boutajangout[1], Arun Paul[1], Ismail Almokyad[1], Iman Mirza[1], Robel Kamal[1], Dalal Alsaggabi[1], Ali Alawami[1], Khadija Al Dhafeeri[1], Aljishi Mohammed[1], Mona Fakhri[1], Amar Aljefri[1], Layla Ghazali[1], Alia Alokley[1], Alan Kozikowski[2], Alan P Kozikowski[2] and **Thomas Wisniewski[1]**
[1]New York University, USA
[2]Alan P Kozikowski, Actuate Therapeutics Inc., USA

Background: Neurofibrillary tangles (NFTs) are constituted of paired helical filaments (PHF), composed of highly phosphorylated forms of the microtubule associated protein tau. The phosphorylation results from the activity of several threonine/serine kinases, and increased expression of glycogen synthase kinase-3β (GSK-3β) has been associated with NFTs. Preclinical and clinical studies have supported that GSK-3β inhibition may have therapeutic potential for AD. Here we assessed the therapeutic effect of our novel GSK-3β inhibitor, ING-135, in an animal model of AD.

Methods: hTau/PS1 mouse model were injected intraperitoneally three times a week with ING-135 (30 mg/Kg; n=15 per group) for three months, while control mice received saline injections.

Results: Treated animals (n=15) didn't show a significant difference compared to controls on sensorimotor tasks (Traverse beam, Rotarod and Locomotor activity). Significant behavioural improvement was noted in treated mice in three tasks using a closed field symmetrical maze (Day 1 two tailed t-test p=0.0072; Day 2 two tailed t-test p=0.0237, Day 3 two tailed t-test p=0.0004). Immunohistochemistry analysis performed on brain sections of treated animals and controls with monoclonal antibodies PHF1 and CP13 showed a reduction of tau pathology in the motor cortex and the hippocampus of treated animals. Further biochemical and immunohistochemical analyses are underway.

Conclusion: A novel inhibitor of GSK-3β (ING-135) improves cognitive decline (long term memory) and decreases tau phosphorylation in treated animals versus controls, in the absence of toxicity.

Biography

Allal Boutajangout obtained a PhD in Neuropathology from Free University of Brussels (ULB-Erasme Hospital), School of Medicine. He has completed his Postdoctoral training at New York University School of Medicine. He is a Research Associate Professor of Neurology and Neuroscience and Physiology. He is also the Chief of the Laboratory of Neurodegeneration and Drug Discovery Program within Center for Cognitive Neurology at NYU. He has received prestigious award Margaret M Cahn for his outstanding research in the field of Alzheimer's and other awards from: Alzheimer association, NIH pilot grant, Toyama Company, Revalesio Company and co-investigator in several RO1 NIH grants. He has published more than 30 papers in reputed journals and serves as a reviewer for many scientific journals.

boutaa01@med.nyu.edu

Notes: