OMICS International
conferenceseries.com

Dong-Gyu Jo et al., Transl Med 2015, 5:4
http://dx.doi.org/10.4172/2161-1025.C1.017

4th International Conference on
Translational Medicine
October 26-28, 2015 Baltimore, USA

Inhibition of Drp1 ameliorates Aβ deposition and restores synaptic depression and memory in Alzheimer's disease model

Dong-Gyu Jo[1], **Hak Kyun Kim**[1], **Gun Young Jung**[1], **Hee Jin Park**[1], **Wook Kim**[2] and **Jae Hyung Park**[1]
[1]Sungkyunkwan University, Korea
[2]Ajou University, Korea

Mitochondrial dysfunction is an early and prominent feature of Alzheimer's disease (AD). In brains of human AD cases as well as AD-like, Aβ plaques are accumulated in mitochondria and may cause structural and functional abnormalities of mitochondria. In addition, mitochondrial abnormalities are found to arise before Aβ plaque deposition. Mitochondria from AD brains show fractured cristae, reduced respiratory capacity and increased mitochondrial fragmentation. Both the treatment of Aβ and the overexpression of Aβ precursor protein (APP) highly induce synaptic injury in neuronal cells as well as massive mitochondrial fragmentation. Exposure to oligomeric Aβ or excessive NO can lead to S-nitrosylation of Drp1 (SNO-Drp1) at Cys644 which activates Drp1 GTPase activity and results in the accumulation of excessively fragmented mitochondria. Moreover, Drp1 activity and the level of SNO-Drp1 were significantly elevated in the brains of sporadic AD cases. Therefore, the adjustment of imbalance of mitochondrial dynamics may have beneficial effects on mitochondrial structure, function and neuronal survival in AD. However, it remains to be determined whether inhibition of excessive mitochondrial fission is beneficial in mammal models of AD. In this study, we evaluated the effect of Drp1 inhibitor mdivi-1 on mitochondrial dysfunction and AD-like neuropathology in APP/PS1 double transgenic AD mice.

jodg@skku.edu

Notes: