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Inhibition of Drp1 Ameliorates Aβ Toxicity in Alzheimer's Disease Model

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Excessive mitochondrial fission is a prominent early event, and contributes to mitochondrial dysfunction, synaptic failure and neuronal cell death in the progression of Alzheimer's disease (AD). In the present study, we examine the role of Drp1, a key regulator of mitochondrial fragmentation, in mitochondrial and synaptic dysfunction-induced by Aβ, and AD-like neuropathology and cognitive functions in AD mice. Our results demonstrate that the treatment of a Drp1 inhibitor, Mdivi-1 alleviates mitochondrial fragmentation, loss of mitochondrial membrane potential, ROS production, and ATP reduction in neurons treated with Aβ oligomers. Furthermore, Drp1 inhibition significantly improves learning and memory, synaptic density, and prevents mitochondrial fission, lipid peroxidation, BACE1 expression and Aβ deposition in an AD mouse model. These results provide evidence that Drp1 plays an important role in Aβ-mediated and AD-related neuropathology, and in cognitive function in an AD animal model. Thus, inhibiting excessive Drp1-mediated mitochondrial fission may be an efficient therapeutic avenue for AD.

Biography:

Dong-Hyung Cho is an Associate Professor in Graduate School of East-West Medical Science at Kyung Hee Universtiy (South Korea). He obtained PhD at Gwangju Institute of Science and Technology at 2005. He was a post-doctoral fellow in Sanford Burnham Preys Medical Discovery Institute in San Diego, USA. He has focused on mitochondrial dynamics and selective autophagy.