MFN2, A Potential Therapeutic Target for Alzheimer's Disease

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Alzheimer's disease (AD) is the most common age-related neurodegenerative disease that affects memory and learning. Mitochondria are critical to neuronal function in the brain, and energy metabolism deficits in the brain have long been documented before the clinical onset of AD, suggesting that mitochondria dysfunction may play an important role in the pathogenesis of AD. Recent data suggest mitochondrial fragmentation in AD likely underlies impaired mitochondrial homeostasis and function in AD. Among the protein regulators of mitochondrial fusion and fission dynamics, mitofusin 2 (MFN2), a mitochondria fusion protein, is significantly downregulated in the brains of AD patients. This could be the reason for mitochondrial fragmentation in AD. In this study, we investigated the effects of MFN2 expression induced by BAY in vitro. Using M17 human neuroblastoma cells, we demonstrated that BAY, a MFN2 inducer, protected M17 human neuroblastoma cells against Aβ-induced cell death. Afterward through BAY injections in 5xFAD mice, an AD mouse model, we explored if BAY could rescue mitochondrial deficits in AD and whether mitochondrial rescue would alleviate other AD-related deficits such as amyloid pathology, oxidative stress, and inflammation. Overall, this study supports the notion that MFN2 is a potential therapeutic target for AD.