

00431 Parkin Regulates Neuronal Lipid Metabolism Through SREBP-LPL Pathway - Implications for Parkinson's Disease

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Aims: Recent studies have pointed out a substantial link between dysregulation of brain lipid metabolism and neurodegenerative diseases. Interestingly, parkin, which is associated with early onset Parkinson's disease (PD), has been reported to regulate fatty acid uptake through CD36 in non-neuronal cells, including cells derived from PD patients with parkin mutations. However, it is currently unclear whether parkin similarly regulates fat metabolism in the brain and whether impairment of its lipidspecific function leads to neurodegeneration seen in PD brains. Therefore, in this study, we aim to elucidate the molecular pathway underlying parkin regulation on brain lipid metabolism.

Methodology: We performed biochemical characterizations and immunofluorescence imaging using samples derived from parkin knockout mouse brains and human neuroblastoma cell lines to identify potential molecular interactors of parkin in the context of brain lipid regulation.

Result: We examined the relationship between parkin level and expressions of protein known to be involved in lipid regulation, such as Lipoprotein Lipase (LPL) and Sterol Regulatory Element Binding Protein 2 (SREBP2), in neuronal cells. Our results reveal a positive correlation between the expressions of these genes and parkin levels, indicating a potential involvement of parkin in modulating brain lipid uptake and/or turnover. In addition, our data show marked reductions in LPL and SREBP2 levels in the brains of parkin knockout mice compared to their wild-type controls. Finally, we demonstrate that disruption of this molecular pathway upon PD-linked stress influences the formation of lipid droplet, an intracellular organelle that has been observed at the onset of neurodegeneration.

Conclusion: In summary, our study unravels a novel molecular pathway involving parkin, SREBP, and LPL in neuronal lipid metabolism. Importantly, these findings open an avenue for new therapy against PD.