Mitophagy modulation as a potential therapeutic target for neurodegenerative diseases

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Résumé

In recent years, it has become clear that even in clinically distinct neurodegenerative diseases, there are common underlying themes in how the neurons become sick and die. One such theme is a breakdown in the maintenance of mitochondria, which plays a central role in neurodegenerative conditions. The selective autophagy of damaged mitochondria (mitophagy) is critical for cell survival as it maintains optimal cellular energy production whilst avoiding the toxic accumulation of damaged mitochondria. Upregulation of mitophagy, and the subsequent restoration of a functional mitochondrial pool, therefore represents a feasible therapeutic strategy for neurodegenerative disease. The successful upregulation of mitophagy requires a deeper mechanistic understanding of this pathway and its upstream regulators, and the development of robust tools and assays to permit experimental interrogation of mitophagy. I will discuss how we overcome these challenges in iPSC-derived neurons, illustrating with ongoing scientific studies in the lab. Our ultimate goal is to identify compounds that are able to modulate mitophagy and rescue mitochondrial pathophysiology and neuronal death.

Mots-Clés: Parkinson's disease, mitophagy

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