POSTER

P75NTR MODULATION IMPROVES RESILIENCE TO OXIDATIVE DAMAGE IN A MICROGLIAL CELL MODEL OF PARKINSON'S DISEASE

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Parkinson's disease (PD) is a progressive disorder associated with an impairment of motor function. Despite its multifactorial etiology, common pathological mechanisms have been recognized, including mitochondrial dysfunction, oxidative stress, lipid dysmetabolism, and neuroinflammation. Collectively, these alterations promote microglial activation and drive the degeneration of neuronal cells. Among neurotrophin receptors, the p75 neurotrophin receptor (p75NTR) has emerged as a key stress-responsive signaling hub involved in both cell survival and pro-apoptotic pathways. We investigated whether pharmacological p75NTR modulation via LM11A-31 could mitigate rotenone (Rot)-induced alterations in BV-2 microglial cells. Rot exposure significantly increased p75NTR expression, suggesting the recruitment of receptor-driven stress signaling under toxic insult. This was accompanied by a profound disruption of mitochondrial architecture, with loss of network complexity and organelle integrity. Such impairment was consistently associated with severe oxidative injury, as demonstrated by enhanced DNA/RNA oxidation and lipid peroxidation. The resulting redox imbalance led to increased apoptosis and evident cytoarchitectural collapse, characterized by altered tubulin disorganization and ultrastructural degeneration. Remarkably, LM11A-31 treatment effectively counteracted Rot-induced pathological cascade, maintaining mitochondrial organization, limiting oxidative damage, reducing cell death, and preserving cell structure. Overall, these findings indicate that Rot triggers a p75NTR-associated degenerative phenotype in microglia, linking bioenergetic failure to oxidative stress and cell death. These results support the potential of LM11A-31 as a candidate for developing innovative therapeutic strategies targeting microglia-mediated mechanisms in PD.

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