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Mitophagy: A Bridge Linking HMGB1 and Parkinson's Disease Using Adult Zebrafish as a Model Organism
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Abstract
High-mobility group box 1 (HMGB1) has been implicated as a key player in two critical factors of Parkinson's disease (PD): mitochondrial dysfunction and neuroinflammation. However, the specific role of HMGB1 in PD remains elusive. We investigated the effect of 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) administration on mitochondrial dysfunction and HMGB1-associated inflammatory genes as well as locomotor activity in zebrafish, aiming to elucidate the role of HMGB1 in PD. Adult zebrafish received MPTP injections, and locomotor activity was measured at 24- and 48-h post-administration. Gene expression levels related to mitophagy (fis1, pink1, and park2) and HMGB1-mediated inflammation (hmgb1, tlr4, and nfkb) were quantified through RT-qPCR analysis. Following MPTP injection, the significant increase in transcript levels of fis1, pink1, and park2 indicated notable changes in PINK1/Parkin mitophagy, while the upregulation of hmgb1, tlr4, and nfkb genes pointed to the activation of the HMGB1/TLR4/NFκB inflammatory pathway. Furthermore, MPTP-injected zebrafish exhibited decreased locomotor activity, evident through reduced distance travelled, mean speed, and increased freezing durations. HMGB1 plays a major role in cellular processes as it is involved in both the mitophagy process and functions as a pro-inflammatory protein. MPTP administration in adult zebrafish activated mitophagy and inflammatory signaling, highlighting the significant role of HMGB1 as a mediator in both processes and further emphasizing its significant contribution to PD pathogenesis. © 2023 by the authors.

Author Keywords
high-mobility group box 1; mitochondrial dysfunction; MPTP; neuroinflammation; Parkinson's disease; zebrafish

Index Keywords
1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine, high mobility group B1 protein, immunoglobulin enhancer binding protein, neurotoxin, toll like receptor 4, transcription factor Nrf2; animal experiment, animal model, animal tissue, apoptosis, Article, brain tissue, cell function, damage-associated molecular pattern-triggered immunity, disability, freezing, gene expression, gene expression level, genetic transcription, histology, locomotion, Locomotor impairment, long term potentiation, mitophagy, nerve degeneration, neurotoxicity, nonhuman, Parkinson disease, protein expression, protein function, real time polymerase chain reaction, respiratory chain, signal transduction, transcription initiation

Chemicals/CAS
1,2,3,6 tetrahydro 1 methyl 4 phenylpyridine, 28289-54-5; neurotoxin, 39386-17-9; toll like receptor 4, 203811-83-0

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