AMPK-mediated Neuroprotection on Cellular Models of Parkinson’s Disease

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ABSTRACT

Objective: To test the neuroprotective effects of AMP-activated protein kinase (AMPK) in Parkinson’s disease (PD) cellular models.

Methods: Regulation of dysfunctional mitochondria, one of the pathogenic mechanisms proposed for PD, may be an effective therapeutic approach in this neurodegenerative disorder. AMPK is a critical regulator of mitochondria in response to energy deprivation. The inactivation of AMPK is associated with increased reactive oxygen species (ROS), decreased ATP levels, and production of pro-apoptotic factors.

Results: Wild-type AMPK, AMPK-T172D mutant (constitutively active AMPK termed as “CA-AMPK”), or AMPK-K157A mutant (domain negative AMPK termed as “DN-AMPK”) constructs were transfected into SH-SY5Y cells. Treatment with wild-type AMPK, AMPK-T172D mutant, or AMPK-K157A mutant significantly increased cell viability and reduced apoptosis compared to control cells. AMPK inhibition with compound C significantly decreased cell viability and increased apoptosis in SH-SY5Y cells.

Conclusions: AMPK activation may have neuroprotective effects on mitochondrial dysfunction-related cell injury.

METHODS

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RESULTS

Mitochondrial dysfunction has been implicated in Parkinson’s disease (PD). AMPK activation reduces ATP deficiency and cytochrome c release, leading to apoptosis. AMPK deficiency activates pro-apoptotic factors and facilitates mitochondrial energy metabolism via SIRT1/PGC-1α signaling pathway and autophagy induction.

REFERENCES


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