

ASK1 in neurodegeneration

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Neurodegenerative diseases (NDDs) such as glaucoma, multiple sclerosis (MS) , Alzheimer's disease (AD) , Parkinson's disease (PD) , amyotrophic lateral sclerosis (ALS) , and Huntington's disease (HD) are characterized by the progressive loss of neurons, causing irreversible damage to patients. Longer lifespans may be leading to an increase in the number of people affected by NDDs worldwide. Among the pathways strongly impacting the pathogenesis of NDDs, oxidative stress, a condition that occurs because of an imbalance in oxidant and antioxidant levels, has been known to play a vital role in the pathophysiology of NDDs. One of the molecules activated by oxidative stress is apoptosis signal-regulating kinase 1 (ASK1) , which has been shown to play a role in NDDs. ASK1 activation is regulated by multiple steps, including oligomerization, phosphorylation, and protein-protein interactions. In the oxidative stress state, reactive oxygen species (ROS) induce the dissociation of thioredoxin, a protein regulating cellular reduction and oxidation (redox) , from the N-terminal region of ASK1, and ASK1 is subsequently activated by the oligomerization and phosphorylation of a critical threonine residue, leading to cell death. Here, we review experimental evidence that links ASK1 signaling with the pathogenesis of several NDDs. We propose that ASK1 may be a new point of therapeutic intervention to prevent or treat NDDs.

<http://www.ncbi.nlm.nih.gov/pubmed/28882588>