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C-Abl inhibition ; A novel therapeutic target for Parkinson 's disease

(Review)

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Abstract

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Parkinson's disease (PD) is the most prevalent movement disorder in the world. The major pathological hallmarks of PD are death of dopaminergic neurons and the formation of Lewy bodies. At the moment, there is no cure for PD; current treatments are symptomatic. Investigators are searching for neuroprotective agents and disease modifying strategies to slow the progress of neurodegeneration. However, due to lack of data about the main pathological sequence of PD, many drug targets failed to provide neuroprotective effects in human trials. Recent evidence suggests the involvement of C-Abelson (c-Abl) tyrosine kinase enzyme in the pathogenesis of PD. Through parkin inactivation, alpha synuclein aggregation, and impaired autophagy of toxic elements. Experimental studies showed that (1) c-Abl activation is involved in neurodegeneration and (2) c-Abl inhibition shows neuroprotective effects and prevents dopaminergic neuronal' death. Current evidence from experimental studies and the first in-human trial shows that c-Abl inhibition holds the promise for neuroprotection against PD and therefore, justifies the movement towards larger clinical trials. In this review article, we discussed the role of c-Abl in PD pathogenesis and the findings of preclinical experiments and the first in-human trial. In addition, based on lessons from the last decade and current preclinical evidence, we provide recommendations for future research in this area. © 2018 Bentham Science Publishers.

Author keywords

Alzheimer's disease | C-abelson | Neurological diseases | Nilotinib | Parkinson's disease | Tyrosine kinase inhibitors

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