Free paper

The potential role of neuroinflammation and transcription factors in Parkinson disease

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Introduction

Parkinson disease (PD) is the second most common neurodegenerative disorder after Alzheimer disease and is characterized by progressive loss of dopaminergic neurons from the basal ganglia, which affects movement control. Bradykinesia, muscular rigidity, resting tremor, and sympathetic instability are primary symptoms of PD, whereas loss of dopaminergic neurons from the basal ganglia—which leads to the biochemical abnormality of low levels of dopamine—and Lewy bodies are the pathological characteristics of PD (*Figure 1*).[1-5] Researchers over the past decade have linked

Parkinson disease (PD) is a neurodegenerative disorder characterized by dopaminergic neurons affected by inflammatory processes. Post-mortem analyses of brain and cerebrospinal fluid from PD patients show the accumulation of proinflammatory cytokines, confirming an ongoing neuroinflammation in the affected brain regions. These inflammatory mediators may activate transcription factors—notably nuclear factor κB, Ying-Yang 1 (YY1), fibroblast growth factor 20 (FGF20), and mammalian target of rapamycin (mTOR)—which then regulate downstream signaling pathways that in turn promote death of dopaminergic neurons through death domain–containing receptors. Dopaminergic neurons are vulnerable to oxidative stress and inflammatory attack. An increased level of inducible nitric oxide synthase observed in the substantia nigra and striatum of PD patients suggests that both cytokine- and chemokine-induced toxicity and inflammation lead to oxidative stress that contributes to degeneration of dopaminergic neurons and to disease progression. Lipopolysaccharide activation of microglia in the proximity of dopaminergic neurons in the substantia nigra causes their degeneration, and this appears to be a selective vulnerability of dopaminergic neurons to inflammation. In this review, we will look at the role of various transcription factors and signaling pathways in the development of PD.

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