The Role of LRRK2 Inhibitors in Treatment of Parkinson’s Disease

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Abstract

Parkinson’s disease is the second most common age associated neuron degenerative disorder in developed societies. With the prevalence ranging from 41 per 100000 in the fourth decade of life to over 1900 per 100000 in people over 80 years of age, it is characterized clinically by resting tremor, slowness of movement, rigidity and postural instability in the result of progressive loss of dopaminergic neurons in the substantia nigra. Although a variety of possible pathogenic mechanisms have been proposed over the years, its etiology has not yet been fully understood. Chronic inflammation is one of the etiologies of Parkinson’s disease and play vital role in the degeneration of dopaminergic neurons. Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene are found in Parkinson’s disease, as in immune related disorder including Crohn’s disease and leprosy. Increasing evidence suggests that LRRK2 protein play an important role in innate immunity. A process that occurs in neurodegenerative disease including Parkinson’s disease.

LRRK2 is a large and complex protein with a unique multiple domain architecture and that can function as a protein kinase with many putative substrates identified and can also function as a GTPase that may serve in part to regulate kinase activity. The combined genetic and biochemical evidence supports a hypothesis in which the LRRK2 kinase function is involved in the pathogenesis of sporadic and familial form of Parkinson’s disease. This finding suggests that LRRK2 kinase inhibitors may potentially offer new treatment for Parkinson’s disease.

Keywords: Neuroinflammation, Parkinson’s disease, LRRK2 inhibitors

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