Parkinson's disease (PD) is one of the most common neurodegenerative diseases in the world, characterized mainly by dopaminergic neuron loss in the substantia nigra pars compacta (SNpc) and the accumulation of ?-synuclein-containing inclusions, named Lewy bodies.Thus, in PD models induced by toxins, both increased Akt and AMPK could negatively regulate the activity of mTOR, leading to the impairment of downstream 4EBP1 and P70S6K-related protein synthesis.This protein synthesis is essential for cell long-term survival.Thus, MPTP is usually used for animal models of PD, and MPP+ is used for cell models of PD. As mTOR signaling is a central hub of signaling networks in cells, it has been widely explored and has been found to have a complex relationship with PD. Both activation and inactivation of mTOR signaling are involved in the different stages of PD. ?-synuclein accumulation is a hallmark of PD, which has been implicated in the pathogenesis of sporadic and familial PD [68,69].Genetic mutations are the leading cause of the disease, but it can also be caused by aging or dopaminergic neuron-specific toxins, such as 6-hydroxydopamine (6-OHDA), 1-methyl-4-phenyl-1,2,3,6 tetrahydropyridine (MPTP), and rotenone [65].An increase in RTP801 expression is also observed in cellular models of PD (6-OHDA, MPP+ or rotenone) and in animal models of PD. In both cases, the increased RTP801 expression is accompanied by decreased mTOR activity [73].The phosphorylation of Akt, the upstream kinase of mTOR, is decreased in the MPP+-induced cellular model of PD, attenuating the activation of mTOR [76].

Summarized by © lakhasly.com