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RTP801 is a critical factor in the neurodegeneration process of A53T α-synuclein in a mouse model of Parkinson's disease under chronic restraint stress

Chen N H, Zhang Zhao, Chu Shifeng and **Wang Zhenzhen**
Chinese Academy of Medical Sciences, China

Background & Purpose: Recently, the incidence of Parkinson's disease has shown a tendency to move younger population linked constantly to the increasing stressors of modern society. However, this relationship remains obscure. Here, we have investigated the contribution of stress and the mechanisms underlying this change.

Experimental Approach: Ten-month-old α-synuclein A53T mice, a model of Parkinson's disease (PD), were treated with chronic restraint stress (CRS) to simulate a PD sensitive person with constant stress stimulation. PD like behavioural tests and pathological changes were evaluated. Differentiated PC12-A53T cells were treated with corticosterone in vitro. We used western blot, microRNA expression analysis, immunofluorescence staining, dual luciferase reporter assay and HPLC electrochemical detection to assess cellular and molecular networks after stress treatment. In vivo, stereotaxic injection of shRNA lentivirus was used to confirm our in vitro results.

Key results: The protein RTP801 is encoded by DNA-damage inducible transcript 4, and it was specifically increased in dopaminergic neurons of the substantia nigra after CRS treatment. RTP801 was post transcriptionally inhibited by the down regulation of miR-7. Delayed turnover of RTP801, through the inhibition of proteasome degradation also contributed to its high content. Elevated RTP801 blocked autophagy, thus increasing accumulation of oligomeric α-synuclein and aggravating endoplasmic reticulum stress. RTP801 inhibition alleviated the symptoms of neurodegeneration during this process.

Conclusions & implications: RTP801 is a promising target for the treatment of PD, especially for PD sensitive patients who live under increased social pressure. Down-regulation of RTP801 could inhibit the current tendency to an earlier onset of PD.

Results and Conclusions:

1. Zhang Z, Chu S F, Wang S S, Jiang Y N, Gao Y, Yang P F, Ai Q D and Chen N H (2018) RTP801 is a critical factor in the neurodegeneration process of A53T alpha-synuclein in a mouse model of Parkinson's disease under chronic restraint stress. British Journal of Pharmacology 175(4):590-605.
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Biography

Chen N H has completed his PhD at the age of 35 years from Saitama University and postdoctoral studies from Mitsubishi. He is the vice director of neuroscience center, Chinese academy of medical sciences, a premier neuroscience research organization. He has published more than 200 papers in reputed journals and has been serving as an editorial board member of repute.

chennh@imm.ac.cn