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Therapeutic relevance of ubiquitin E3 ligase, chaperones and bioflavonoids in neurodegenerative disorders

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Intracellular accumulation of A β 42 is an early event in the pathogenesis cascade of Alzheimer's disease (AD) causing neuronal dysfunction, synaptic and neuronal loss together with dementia. A bifunctional protein C-terminus Hsp70 interactive protein (CHIP) is considered as a connecting link between molecular chaperones and Ubiquitin Proteasome System (UPS) while another E3 ligase Parkin targets several proteins for UPS degradation. Further Parkin's mutations are the major cause of autosomal recessive Parkinson's disease (ARPD) where Parkin catalyzes the post-translational modification of proteins with polyubiquitin targeting them to the 26S proteasome. In addition, Parkin together with CHIP reduces intracellular A β 1-42 peptide levels, an important peptide that shares a cross talk between Alzheimer's and Parkinson's diseases. These ligases counteract its effects on cell death and reverse its effect to inhibit the proteasome. Herein, we reported the implication of CHIP and Parkin in the metabolism of β -amyloid precursor proteins (β APP) and its derivative β -amyloid. We also proved a strong interaction between β -APP, CHIP and HSPs. Interestingly CHIP also promotes the association of ubiquitin with β -APP in proteasomal dependent manner. CHIP together with another Parkin enhances the A β degradation and eliciting neuro protective properties while Parkin alone consider as an inducers of amyloid clearance, a cryoprotectant and in the suppression of reactive inflammation. Furthermore, we have shown the effect of bioflavonoid in the attenuation of hypoxia and neurotoxin induced neurodegeneration in the rat model.

Biography

Pravir Kumar is an Associate Professor in the Department of Biotechnology at DTU. He has obtained MS degree from BHU, Varanasi and PhD degree from Germany in Cardiovascular Physiology. Before returning to India, he has spent several years in the Neurology Department at Tufts University School of Medicine, USA as a Postdoctoral Fellow and later held Faculty Position. Still, he is holding an Adjunct Faculty status in the Neurology Department at Tufts University School of Medicine (TUSM). His areas of research interest and expertise include molecular chaperone and ubiquitin E3 ligase in neurodegenerative disorders along with aberrant cell cycle re-entries into aged neurons and muscles. He is an Editorial Board Member in *Journal of Alzheimer's disease* (IOS press, commencing from Jan 01/2015), *International Journal of Neurology Research*, *American Journal of Research Communication* and Reviewer of several leading Elsevier journals. He has published 37 papers in peer-reviewed journals (Scopus h-index-10; cumulative impact factors: 90; citation index is 925). He has successfully completed LSRB-DRDO funded research defense project on hypoxia induced neurodegeneration in India.

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