Abstract

Proteins are major catalytic biomolecules of the cells that are maintained in their dynamic steady state levels by regular renewal. Cells achieve this through synthesizing new proteins and degrading damaged or misfolded proteins. Improper or poor folding of nascent polypeptide generates a continuous cytotoxic threat. Misfolded proteins, if accumulated, may cause malfunctionality, and subsequently cell death. Neurons are post-mitotic cells, hence are more vulnerable towards such cellular insult. The basic mechanism of protein quality control system, comprising of folding and degradation machinery, is however known, yet the details of all its components and comprehensive mechanism as well as the interplay remain obscure.

Current study reveals that Mahogunin Ring Finger 1 (MGRN1), an E3 Ubiquitin ligase, earlier found to be involved in mouse coat color, is sensitive to cytotoxic stresses and gets elevated in these conditions. The current investigation explores the role of MGRN1 as a novel protein quality control E3 Ubiquitin ligase and shows that it suppresses the misfolded protein aggregation and cytotoxicity. MGRN1 interacts with Hsp70 protein in cells. All such characteristics have generated scope to investigate the role of MGRN1 in neurodegenerative diseases and interestingly, it was observed through the studies on polyglutamine proteins that MGRN1 suppresses the expanded polyglutamine protein aggregation. MGRN1 was also found to be associated with the polyglutamine aggregates in Huntington disease model mice brain. Investigating such novel quality control E3 Ubiquitin ligases may add to our knowledge about protein quality control system and neurodegeneration, which may in turn help in developing therapeutics to such devastating pathological conditions.