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Conclusion

The whole study leads to an indication that Mahogunin RING Finger 1 E3 Ubiquitin ligase can serve as a quality control E3 Ubiquitin ligase which associates and interacts with misfolded proteins. MGRN1 promotes the degradation of misfolded proteins and this functionality of MGRN1 is enhanced in the presence of Hsp70 chaperone. MGRN1 also associates and interacts with Hsp70 chaperone. MGRN1 protein's strong association with misfolded protein aggregates along with ubiquitin, Hsp70 and p62 indicates that the E3 Ubiquitin ligase may be involved in the degradation of these misfolded proteins through autophagy pathway. The current study indicates that the recruitment of MGRN1 with expanded polyglutamine proteins occurs in cellular and mice models of HD disease. Together, these results suggest that MGRN1 interacts with expanded polyglutamine proteins; the association of MGRN1 promotes the ubiquitination and elimination of polyglutamine expansions that eventually alleviate aggregation and cell death. MGRN1 provides cytoprotection against expanded polyglutamine induced toxicity and probably its aberrant function plays a crucial role in the pathomechanism of neurodegeneration and possibly holds therapeutic potential for treating protein-disordered diseases.

The identification of an E3 Ubiquitin ligase that is capable of eliminating misfolded aggregated proteins represents a potential therapeutic approach against diseases caused by disordered proteins. There are numerous studies implicating autophagy or selective autophagy in polyglutamine diseases. However, the detailed molecular function of autophagy in the selective recognition of expanded polyglutamine proteins is still not well understood. This study, hereby, has aided the knowledge of protein quality control system, and presented a novel role of MGRN1 in misfolded protein clearance and its role in polyglutamine diseases. This study extends the possibilities of investigations in protein quality control function of E3 Ubiquitin ligases which may serve as important sources of knowledge that could be helpful in finding novel therapeutics for neurodegeneration.

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