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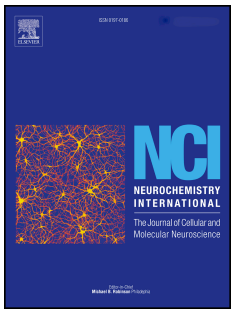

PQBP1, an intrinsically disordered/denatured protein at the crossroad of intellectual disability and neurodegenerative diseases

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PQBP1, an intrinsically disordered/denatured protein at the crossroad of intellectual disability and neurodegenerative diseases

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Abstract

PQBP1 (polyglutamine binding protein-1) is the earliest identified molecule among the group of disease-related intrinsically disordered/denatured proteins. PQBP1 interacts with splicing-related factors via the disordered/denatured domain and regulates post-transcriptional gene expression. The mutations cause intellectual disability due to decreased dendritic spines and abnormal expression of synapse molecules in neurons, and microcephaly due to elongated cell cycle time and abnormal expression of cell cycle proteins in neural stem progenitor cells. Meanwhile, PQBP1 interacts with polyglutamine tract sequences translated from CAG triplet disease genes via their disordered/denatured structures. The second hit on PQBP1 by such neurodegenerative disease proteins is supposed to similarly impair synapse functions in neuron and proliferation of stem cells. The alteration of gene expression profile and consequently induced phenotypes of neuron and stem cells via secondary impairment of the intrinsically disordered/denatured protein PQBP1, which are similar to developmental disorders by PQBP1 gene mutations, could be a part of the main pathologies shared by multiple neurodegenerative diseases.

KEY WORDS

PQBP1; intrinsically disordered/denatured protein; intellectual disability; neurodegenerative disease; RNA splicing; transcription