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INTERACTION OF PRION PROTEIN WITH MICROTUBULES

Summary

Misfolded prion protein (PrP^{TSE}) is known as a major agent leading to infectious neurodegenerative diseases, known as transmissible spongiform encephalopathies (TSE). The mechanism of conversion of the physiological form of prion protein (PrP^{C}) into the pathological PrP^{TSE} as well as the identity of neurotoxic form of this protein is not fully characterized. Under physiological conditions, PrP^{C} one, is predominantly extracellular, tethered to the plasma membrane surface through the GPI anchor. However, cytosolic forms of PrP, termed as cytoPrP have also been found. Interestingly, a significant increase in the concentration of cytoPrP is observed in TSE. Recently, it was shown that mislocalized PrP can be a neurotoxic agent. The mechanism of neurotoxicity might be linked to the direct interaction of this form of PrP with tubulin. This interaction leads to tubulin aggregation, inhibition of microtubules (MT) assembly, disruption of microtubular cytoskeleton and eventually cell death. MT stabilization, by decreasing the level of MAP phosphorylation, can protect neurons from toxic effect of cytosolic forms of PrP.

Key words: microtubules, prion diseases, prion protein, tubulin