FUNCTIONAL STUDY OF CELLULAR PRION PROTEIN MUTANTS LOCALIZED IN OR NEXT TO THE LAMININ INTERACTION SITE

COOK, Z.S.P., MACHADO, C.F.M, PEREDA, P.A.L., MARTINS, V.R.
LICR, São Paulo, Brazil

Prion diseases are neurodegenerative encephalopathies that can have infectious, sporadic or inherited origin and affect both animals and humans. Since the identification of the cellular isoform (PrP^c) of the prion protein and its corresponding gene, more than 55 mutations were described as related to pathologies. Many physiological functions of PrP^c have been described that could be hampered by disease related mutations, suggesting a PrP^c loss-of-function in the disease. We constructed a GFP-PrP^c quimera containing the mutations V180I, T183A and E200K on the prion protein, localized in or near its laminin binding site, previously described as required for neuronal adhesion and differentiation. Using confocal microscopy, we show that similarly to the wild-type protein, PrP^{V180I} and PrP^{E200K}, are localized to the plasma membrane and perinuclear region. Interestingly, PrP^{T183A} accumulates at perinuclear region, suggesting retention in the endoplasmic reticulum. Migration assays using laminin were performed with N2a cells stably transfected with GFP-PrP^c mutants. No significant differences were detected on the migration rates of the mutants comparing to the wild-type protein. Further work, with different approaches, should be addressed for a better evaluation of the impact of mutations on the normal functions of the cellular prion protein.

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