CELLULAR PRION PROTEIN MUTATIONS IMPAIR CELL MIGRATION MEDIATED BY LAMININ

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Cellular prion protein (PrPc) gene (*PRNP*) mutations are involved in neurodegenerative disorders collectively called Transmissible Encephalopathies (TSEs). PrPc is a glycoprotein abundantly expressed on the surface of neuronal and glial cells. Several reports point out to the PrPc participation in neuronal adhesion and cell differentiation through its interaction with the extracellular matrix protein Laminin (Ln). Interestingly, a *PRNP* polymorphism (codon 171) and a specific PrPc mutation (codon 178), the latter associated to a inherited form of prion disease, are located inside or close to the PrPc-Ln binding domain (174 to 181, in human molecule). To investigate if these PrPc polymorphism/mutation interfere with PrPc binding to Ln and consequently with the biological functions of this interaction, we constructed vectors which express PrPc mutants ($PrPc^{171S}$ and $PrPc^{178N}$) fused to green fluorescent protein (GFP) that were transfected into neuronal cell lines. As observed through confocal images, wild-type GFP-PrPc, as well as all PrPc mutant constructs, discloses a normal distribution on the cell surface and in the Endoplasmic Reticulum/Golgi Complex. To evaluate if PrPc mutations impairs cell migration mediated by laminin, N2a cells expressing theses constructs were used. When compared to wild-type ones, the cells expressing PrPc mutants show a 80% lower cell migration. Taken together, these data suggest that PrPc mutation at the Ln binding domain may results in the impairment of important cellular functions.

Supported by FAPESP and HHMI