EVALUATION OF PRION PROTEIN INTERACTION WITH DNA: CALORIMETRIC ANALYSES AND CELLULAR TOXICITY ASSAYS

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Prion diseases (transmissible spongiform encephalopathies) are neurodegenerative disorders caused by a pathogenic isoform of the prion protein, denominated PrP^{Sc}. This isoform is protease-resistant, forms amyloid fibrils and has high ß-sheet content. The cellular prion protein (PrP^{C}), a highly conserved cell surface glycoprotein, is protease-sensitive and has high a-helix content. Several biological ligands of PrP have already been identified, with distinct implications for PrP function and conversion to PrP^{Sc}. Among these ligands, nucleic acid molecules are putative candidates to participate in the PrP conversion. In the present work, we evaluated by MTT reduction assays the cytotoxicity to neuroblastoma cell culture of PrP:DNA complex and of PrP aggregates formed upon high-temperature incubation and further submitted to high-hydrostatic pressure. Our results showed that under the conditions tested for aggregation, PrP forms amyloid fibers and, in some situations, acquires cytotoxicity. We also aimed to characterize the thermodynamics of the PrP:DNA complex formation by isothermal titration calorimetry (ITC) and differential scanning calorimetry (DSC). The calorimetric data may contribute to a better understanding about the interaction and stability of PrP complexed with this biological ligand. Those interactions can be the key for illumination of mechanisms involved in prion diseases, which affect humans and other mammals.

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