Heparin Binding Increases Murine Prion Protein Stability

Vieira, TCRG1, Gomes, MPB1, Cordeiro, Y2 & Silva, JL1.

1 Instituto de Bioquímica Médica, 2 Faculdade de Farmácia, Universidade Federal do Rio de Janeiro, Brasil.

The conversion of PrP into scrapie PrP is the central event of prion diseases. A series of molecules have been considered to work as adjuvants in the conversion process, including glycosaminoglycans (GAGs) (1). Some authors have suggested that these molecules directly convert the protein into a protease resistant form, while others have proposed that these molecules block the interaction of PrP with endogenous GAGs, resulting in a protective activity. Our group recently reported that low molecular weight heparin (LMWHep) does not induce recombinant murine prion protein (rPrP23-231) conversion, protecting rPrP23-231 from RNA-induced aggregation (2). We asked whether LMWHep increases murine prion protein stability, changing its ability to aggregate. In the present work, high temperatures, amyloid fibril conversion in vitro assay, and synthetic peptides were used to investigate changes in protein stability and tendency to aggregate triggered by LMWHep interaction. We show that formation of LMWHep-rPrP 23-231 complex increases rPrP 23-231 stability, decreasing temperature-induced aggregation and amyloid fibril formation. Our findings may explain the protective effect of these molecules in different models.

References:


Keywords: Prion, Gycosaminoglycan, Aggregation, Neurodegeneration
Supported by CNPq, MS/DECIT and FAPERJ.