Structural Analysis of Prion Fibrils Induced by Phosphatidic Acid.

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INTRODUCTION: Transmissible spongiform encephalopathies are a group of fatal diseases, which affect mammals, caused by an abnormal isoform of the prion protein (PrP). Conversion of cellular PrP (PrP^C) into the pathological conformer, PrP^{Sc}, involves contact between both isoforms and probably requires a cellular factor. Recombinant PrP can be converted to an abnormal form via seeded polymerization *in vitro* techniques in the presence of lipids. **OBJECTIVES:** The importance of lipid molecules for conversion has been revealed, but little is known about the structural features implicit in this interaction. A detailed understanding of PrP aggregates assembly and disassembly is important to understand a key event in prion diseases. **MATERIAL AND METHODS:** In the present work, we used light scattering, circular dichroism and fluorescence measurements in order to provide information on the structure and stability of recombinant PrP fibrils formed by binding to Phosfatidic Acid (PA) vesicles. **RESULTS AND DISCUSSION:** We found that PA induces changes on PrP^C secondary structure, increasing β-sheet structure, forming fibrils. This effect was major at low temperatures. High temperatures did not disassemble these fibrils, whereas remodeled. **CONCLUSIONS:** Our results suggest that PA triggers PrP^C aggregation, generating stable fibrils with an intermediate secondary structure, between PrP^C and PrP^{Sc} , which can be remodeled by temperature.

Key words: Prion conversion, Aggregation, Phospholipid.
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