INTERACTION OF PRION PROTEIN WITH RNA AND DNA: A CROSSROAD BETWEEN THE PROTEIN AND NUCLEIC ACID WORLDS

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The main hypothesis for the pathogenesis of transmissible spongiform encephalopathies (TSE) proposes that the cellular prion protein (PrP^{C}) can be altered into a misfolded, □-sheet-rich isoform (PrP^{Sc}). There is no doubt that the infections material of prion diseases consists basically of the prion protein with no nucleic acid, in contrast to a virus particle, which has both. Howeve, many studies show that prions have other accomplices that chaperone their activity in converting the normal, cellular form into the disease-causing isoform. Our studies and from other groups show that among chaperone candidates, a nucleic acid (RNA or DNA) is the most likely. The main hypothesis for the mechanism is that nucleic-acid binding reduces the protein mobility and therefore makes the protein-protein interactions more likely (*J Biol Chem* 2001, 276: 49400-9). We summarize the findings, focusing in the biological relevance of the nucleic acid catalytic action. Small-angle X-ray scattering (SAXS) and nuclear magnetic resonance spectroscopy measurements reveal that the globular domain and the unstructured N-domain of PrP participate importantly in the formation of the complex (*Biochemistry* 2006, 45: 9180-7). The structural visualization of the complex provides insight into how oligonucleotides bind to PrP and opens new avenues to the design of compounds against prion diseases. The elusive function of the prion protein may reside in the interaction of PrP protein with a nucleic acid, not related with its coding sequence, but involved in replication of PrP. Supported by CNPq, FAPERJ and FINEP.
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