PrP:RNA INTERACTION GENERATES TOXIC SPECIES

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Prion diseases are triggered when the cellular prion protein (PrP^C) changes from its α-helical into a β-sheet-rich structure, generating PrP^{Sc}, the only known component of the infectious prion particle. The main hypothesis for prion diseases proposes that $PrP^C \rightarrow PrP^{Sc}$ conversion occurs without the participation of any other molecule. However, it is also believed that an additional factor may be involved in this transition, lowering the energy barrier between PrP^C and PrP^{Sc}. Our previous findings demonstrated that PrP interacts with nucleic acids *in vitro*, binding small sequences of dsDNA, acquiring β-sheet secondary structure. Other works showed that PrP interacts with RNA and becomes resistant to protease digestion. In this work we report experimental data on the interactions between PrP and RNA, focusing on secondary and tertiary structural changes. We also investigated the role of the N-terminal region of PrP in RNA binding and evaluated the toxicity of the PrP:RNA complex in cultured neuroblastoma cells (N2a). Our results showed that RNA binding induces lost of α-helical content, leads to PrP aggregation and the N-terminal domain seems to be important to this interaction. We also observed that aggregates generated upon PrP:RNA interaction are toxic to N2a cells, suggesting that RNA molecules are strong candidates for catalyzing prion conversion.

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