INTRODUCTION: Prion proteins (PrPs) are involved in lethal neurodegenerative diseases, that affect humans and other animals. So far, many issues remain unclear about PrP physiopathological role. The misfolding of its normal cellular form (PrP\textsuperscript{C}) into an abnormal form (PrP\textsuperscript{Sc}) characterizes the central event of these pathogenesis. Some studies have suggested nuclear localization for PrP\textsuperscript{C} and functions derived from its interaction with nuclear components. Having a common place to cross-talk, nucleic acids (NAs) are intriguing PrP molecular partners, and have been proposed as cofactors in the protein misfolding process. OBJECTIVES: We aim to clarify the biological relevance of PrP-NA interactions.

MATERIALS AND METHODS: We studied the binding of several oligonucleotides (RNA and DNA) with the recombinant murine PrP (rPrP) through isothermal titration calorimetry (ITC) and spectroscopy assays. We performed different cellular assays to evaluate cytotoxicity and cell viability, working with two cell lineages (neuroblastoma - N2a - and kidney cells – HK2). We also worked with a well-known neurotoxic human prion peptide (PrP\textsuperscript{106-126}) upon its interaction with these oligonucleotides.

RESULTS AND DISCUSSION: We found that interactions of rPrP or PrP\textsuperscript{106-126} with NAs can lead to different aggregates and neurotoxic species, depending on the NA molecule. Interestingly, the N2a cells morphology changed in the presence of the cytotoxic PrP-NA complexes, which indicate that they are indeed affecting cell signaling. The preliminary in vivo results of the intracerebral inoculation of a rPrP-DNA complex in healthy mice (C57BL/6) indicate significant impairment of memory consolidation, although there was no apparent locomotors dysfunction in these mice through extensive behavioral tests.

CONCLUSIONS: Our results showed the NA ability of binding to rPrP, induce conformational changes, modulate protein aggregation and cytotoxicity in vitro and to induce neurological damages in vivo. Understanding the structural, cellular and in vivo effects observed for PrP and NAs interactions may enlighten the still obscure prion physiopathology and many others neurodegenerative diseases.

Keywords: prion protein, nucleic acids, interaction, neurodegenerative diseases

Support: CAPES, FAPERJ and CNPq

Este é apenas um modelo, todo o texto deve ser escrito em INGLÊS.