INTRODUCTION: Prion diseases are fatal neurodegenerative protein-misfolding diseases related to a protein known as prion protein (PrP). The constitutive cellular isoform of PrP (PrP<sup>C</sup>) present in cell surface, can be converted into its abnormal, β-sheet-rich isoform (PrP<sup>Sc</sup>) that undergoes aggregation. PrP<sup>Sc</sup> can be transmissible and infectious. Evidences suggest that cofactors may play a role in the conversion process. Our group previously reported that DNA can convert PrP<sup>C</sup> into the β-sheet conformation leading to aggregation[1]. Innate immune system cells have been proven to play critical roles in the early events of prion diseases and may be involved in its progression[2]. Following peripheral exposure, the replication of prions within lymphoid tissue has been shown to be important for the efficient spread of the disease to the brain. Neutrophil extracellular traps (NETs) are large DNA networks decorated with histones and granule proteins that trap and kill pathogens, being extruded by activated neutrophils in response to several stimuli. Furthermore NETs were recently found in association with amyloid fibrils in tissues of patients with other protein-misfolding diseases and these fibrils triggered the release of NETs[3]. Regarding these observations and considering the large quantity of DNA provided by NETs we asked if NETs could induce PrP<sup>C</sup> aggregation <i>in vitro</i>. MATERIALS AND METHODS: Murine recombinant PrP(23-231) was added into the supernatant from activated human neutrophils NETs to measure and characterize aggregation. RESULTS AND DISCUSSION: NETs dose-dependently triggered an instantaneous PrP<sup>C</sup> aggregation which decreased over time due to protease activity in NETs. The aggregates showed amorphous morphology and absence of fibrils. NETs previous treatment with DNase I inhibited PrP<sup>C</sup> aggregation, pointing out the importance of the DNA integrity for its effect. CONCLUSION: Our data suggest that NETs are an intriguing factor that must be appraised in studies concerning prion propagation mechanisms.


Palavras chave: prion, neutrophil extracellular traps, protein aggregation, neutrophil