Prion Protein Aggregation Triggered By Neutrophil Extracellular Traps (NETs)

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INTRODUCTION: Prion diseases are fatal neurodegenerative protein-misfolding diseases related to a protein known as prion protein (PrP). The constitutive cellular isoform of PrP (PrPC), present in cell surface, can be converted into its abnormal, β-sheet-rich isoform (PrPSc) that undergoes aggregation. PrPSc can be transmissible and infectious. The evidences so far suggest that adjuvant factors, such as glycosaminoglycans and nucleic acids, may play a role in the conversion process. Our group previously reported that DNA can convert PrPC into the β-sheet conformation leading to aggregation. Neutrophil extracellular traps (NETs) are large DNA webs decorated with histones and granule proteins released by neutrophils that trap and kill pathogens. Recently, NETs were found in association with amyloid fibrils in tissues of patients with other protein-misfolding diseases. Furthermore, amyloid fibrils triggered the release of NETs [1]. 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. Moreover, NETs were reported of being released in lymphoid tissues. Regarding these observations and considering the large quantity of DNA provided by NETs we asked if NETs could induce PrPC aggregation in vitro. MATERIALS AND METHODS: Murine recombinant PrP (23-231) was added into the supernatant from activated human neutrophils containing NETs. Aggregation was measured by turbidimetry (330 nm) and electron microscopy. RESULTS AND DISCUSSION: Aggregation was detected and reached a maximum after the first 10 minutes of incubation and then gradually declined remaining detectable after 1 hour. The aggregates showed amorphous morphology. This results report that NETs can trigger a stable aggregation of PrPC. However, fibrillar structures were not detected. CONCLUSION: Our data suggest that NETs are an intriguing factor that must be appraised in the studies concerning prion propagation mechanisms.


Palavras chave: prion, neutrophil extracellular traps, aggregation, neutrophil
Patrocínio: FAPERJ, CNPq, PRONEX, CAPES, IMBEBB