Spreading of Misfolded Protein Aggregates as a Pathogenic Mechanism of Neurodegenerative diseases

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Misfolded protein aggregates are implicated in most neurodegenerative diseases, including Alzheimer’s, Parkinson’s, Huntington’s disease, Amyotrophic Lateral Sclerosis, and prion disorders. Despite the differences in clinical manifestation, these diseases share as a hallmark event the misfolding of a protein to form β-sheet rich aggregates that deposit in diverse regions of the brain inducing neuronal death and synaptic dysfunction. Among neurodegenerative diseases, prion disorders are unique in that the pathology can be transmitted by an infectious process involving a heretical agent known as prion. Prions are infectious proteins capable to transmit biological information by propagation of protein misfolding and aggregation. The hypothesis that prions are composed exclusively by a protein with the unprecedented ability to behave like a micro-organism was controversial during decades, but recent studies have settled all doubts.

The process of protein misfolding and aggregation follows a seeding-nucleation mechanism in which small oligomers act as seeds to trigger an uncontrolled aggregation process. The seeding mechanism appears to be the basis by which misfolded prion protein propagates prion disease in an infectious manner. The inherent infectious nature of misfolded aggregates propagating by a seeding mechanism suggests that other neurodegenerative diseases may be transmissible in the same manner as prion disorders. In this presentation, we will show evidences that the pathology of Alzheimer’s disease can be also experimentally transmitted in vivo and highlight the prion properties of amyloid-beta aggregates. These findings may change our understanding of these diseases and provide novel strategies for treatment.