

Are amyloids infectious? Prions and prion-like proteins: myths and facts.

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Transmissible Spongiform Encephalopathies (TSEs) or prion diseases are a group of fatal neurodegenerative disorders affecting mammals. Albeit their low incidence in humans, prion diseases are a subject of passionate research due to their unorthodox mechanisms of transmission mediated by misfolded proteins, and the zoonotic potential of Bovine Spongiform Encephalopathy (BSE or "mad cow" disease). Importantly, prion diseases in deer and sheep can be prevalent and persistent, raising important concerns in terms of public health due to their uncontrolled spread and possible transmission to humans. Importantly, the accumulation of misfolded protein aggregates is not an exclusive feature of TSEs, but also present in several other pathological conditions including Alzheimer's Disease (AD), Parkinson's disease, type-2 diabetes, and others. Recent reports suggest that the spread of misfolded proteins and further pathological features in these diseases operates in a similar manner as seen for infectious prions. This has opened controversial and prolific lines of investigation that are currently being explored by several research groups around the world.

My laboratory focus on i) investigating the molecular mechanisms dictating prion pathogenicity, ii) the development of diagnostic methods against prion diseases, iii) the prion-like properties of misfolded amyloid- β protein (associated to AD), among other topics. In this presentation, I will focus on recent advances for prion detection in Chronic Wasting Disease (CWD), a TSE of cervids. In addition, mechanistic aspects of CWD transmission will be discussed, including horizontal and environmental transmission, role of prion protein polymorphisms in prion strain variation, and others. The second part of my talk will center on our research exploring whether features that define prions as infectious agent exist on AD's amyloid- β . Specifically, the possibility of inter-individual transmission, presence of conformational strain variation, etc. on misfolded amyloid- β will be discussed. My aim in this talk is to highlight the common mechanisms of spread for prions and amyloid- β , and suggest common strategies for early diagnosis based in the prion-principle.