Subviral Pathogens and the Development of the Prion-Concept for Neurodegenerative Diseases

Small naked RNAs without coding capacity were identified as pathogens of some plant diseases in the late sixtieth/early seventieth. They posses features of viruses like infectivity and pathogenicity, and were coined viroids by their discoverer Ted Diener ( ). Scientists argued that other unidentified pathogens like those of scrapie of sheep and human diseases like Kuru and Jakob-Creutzfeld disease could be viroid-like ( ). Mainly the studies of Stanley Prusiner identified the scrapie agent as a proteinaceous particle called prion. The main component of the prion is the host encoded prion protein which can exist in a cellular, non-pathological conformation (PrPc) or in anaggregated pathological conformation PrPSc. If PrPC encounters incoming PrPSc during infection, PrPSc forces PrPC to misfold into the pathological isoform PrPSc thereby amplifying the infectvity. This concept of induced misfolding underlies also formation and expansion of pathological Aβ-oligo -and polymeric aggregates in Alzheimer’s disease, α-synuclein aggregates in Parkinson’s disease and other neurodegenerative diseases. What started with the search for viroid-like pathogens led to the development of therapeutic concepts for neurodegenerative diseases.