

## **Transmission of misfolded proteins in neurodegenerative disorders: a common mechanism of disease progression**

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The deposition of  $\beta$ -sheet rich amyloid aggregates formed by disease-specific proteins is a common feature of many neurodegenerative diseases and are believed to cause neuronal dysfunction directly or indirectly. Recent studies have strongly implicated cell-to-cell transmission of misfolded proteins through templated recruitment as a common mechanism for the onset and progression of various neurodegenerative disorders. Emerging evidence also suggests the presence of conformationally diverse “strains” for each type of disease protein, which may be another shared feature of amyloid aggregates, accounting for the tremendous heterogeneity within each category of diseases. In Alzheimer’s disease and other age-related tauopathies, the normally soluble tau protein accumulate as insoluble neurofibrillary tangles whereas in Parkinson’s disease and other related synucleinopathies, the highly soluble  $\alpha$ -synuclein protein are converted to aggregated Lewy bodies in neuron and glia. Finally, in FTLD-TDP and ALS, TDP-43 forms aggregates in brain and spinal cord. We have developed mouse models of these neurodegenerative diseases and have used them to test the “transmission” hypothesis and the “strain” hypothesis in order to elucidate mechanisms of progressive spread of these pathology as well as to explore the molecular basis of strain heterogeneity.