

Summerlee Science Complex SSC 2315

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Strains of Pathological Protein Aggregates in Neurodegenerative Diseases

A defining feature of neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease (PD) is the presence of pathological protein aggregates within the brain. Evidence is accumulating that several neurodegenerative dis-

ease-associated proteins, such as A β in AD and α -synuclein in PD, can polymerize into distinct "strains" of aggregates. Prion strains, which are encoded by different conformations of protein aggregates, underlie the clinical and pathological heterogeneity observed amongst prion disease subtypes. We have hypothesized that distinct strains of A β and α -synuclein may be responsible for enciphering disease variability in AD, PD, and related neurological disorders. Using transgenic mouse models of AD and PD, we have shown that distinct diseases can be induced by injection with unique aggregate strains. Strain-specific differences were maintained after serial passaging suggesting that A β and α -synuclein strains propagate within the brain via prion-like conformational templating. Thus, the existence of protein aggregate strains provides a plausible explanation for the disease heterogeneity observed among human neurodegenerative disorders.