

Structural Studies of Prion Fibrils and Other Protein Fibrils

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Research Abstract

Progress in FY2065 was in the following areas: LOW COMPLEXITY SEQUENCES. In collaboration with Prof. Steven McKnight (UT Southwestern Medical Center) and his colleagues, we have performed solid state NMR measurements on fibrils formed by low complexity (LC) sequences of hnRNPA2 and FUS, which are likely to be related to protein aggregates implicated in ALS, FTD. For both hnRNPA2 and FUS LC fibrils, 2D and 3D solid state NMR spectra indicate that only a fraction (20%) of the LC sequence forms the fibril core, with the

remaining segments forming flexible loops outside the core. Solid state NMR measurements show that the core is an in-register, parallel cross-beta structure, as in many amyloid fibrils. Chemical shift assignments have been obtained for FUS LC fibrils, showing that approximately 35 residues are contained in the immobilized fibril core. Mass-per-length measurements by dark-field transmission electron microscopy indicate a single FUS LC molecule in each repeat unit along the fibril axis. Additional solid state NMR measurements to develop a full structural model are in progress.

Further information available at:

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United States of America

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