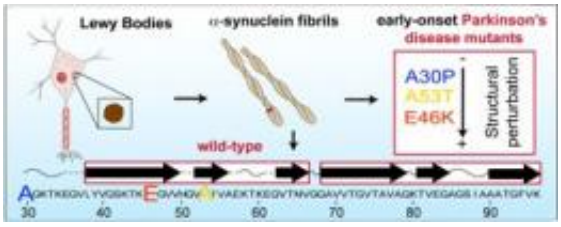
Finding key structural insights into the pathological hallmark of Parkinson's disease

September 27 2011



Better understanding the structure of AS fibrils is a step toward finding a treatment for Parkinson's disease.

A team of researchers from the University of Illinois and EMSL recently completed a detailed structural and dynamic characterization of full-length α-Synuclein (AS) fibrils.

AS fibrils are the major component of Lewy bodies, the pathological hallmark of Parkinson's disease, which affects approximately 1–2% of the population over age 65.

By applying state-of-the-art, solid-state nuclear magnetic resonance (NMR) capabilities at EMSL, including the 900-MHz NMR spectrometer, as well as improved sample preparation and labeling schemes, the researchers detected many previously unobserved residues in the fibrils and performed detailed analysis of the side chains as well as the backbone.

The team's results show that the core extends with a repeated structural motif and that three single-point mutations associated with early-onset Parkinson's disease —A30P, E46K and A53T—are located in structured regions. Additionally, the researchers found that E46K and A53T mutations are associated with major and minor structural perturbations, respectively.

These results are a step toward the rational design of small molecules to diagnose and/or treat Parkinson's disease and present a new approach for discovering therapeutic targets.

More information: Comellas G, LR Lemkau, AJ Nieuwkoop, KD Kloepper, DT Ladror, R Ebisu, WS Woods, AS Lipton, JM George, and CM Rienstra. 2011. "Structured Regions of [Alpha]-Synuclein Fibrils Include the Early-Onset Parkinson's Disease Mutation Sites." *Journal of Molecular Biology* 411:881-895. DOI:10.1016/j.jmb.2011.06.026

Provided by Environmental Molecular Sciences Laboratory