J Neurol Disord 2018, Volume 6
DOI: 10.4172/2329-6895-C6-041

Newly discovered Parkinson disease-associated mutations result in faster aggregation of α-synuclein and exhibit cytotoxicity

Deepak Kumar Jangir
Regional Centre for Biotechnology, India

Parkinson disease (PD) is a progressive movement disorder, affecting millions of people worldwide. Mutations that cause abnormal aggregation of α-synuclein have a close association with the onset of PD and its progression. Therefore studies pertaining to α-synuclein mutations play important roles in the mechanistic understanding of aggregation behavior of the protein and subsequent pathology. In the present study, we have shown that two newly discovered PD associated mutants, A18T and A29S, significantly modulate the aggregation behavior of α-synuclein. The results presented here indicate that A18T is highly aggregating in nature, while A29S have similar albeit weaker tendency. We further demonstrate that substitution of alanine at 18th position is highly devastating compared to adjacent positions. This study illustrates that some amino acid positions could be treated as a hot spot for α-synuclein aggregation while others could be less sensitive towards substitutions. Moreover, cytotoxic effects of fibrils and oligomers of these mutants have been assessed by MTT assay and it found that oligomers of mutant proteins are highly cytotoxic compared to mature fibrils. The present study provides detailed insight into the aggregation behavior of two newly discovered PD associated mutants and their possible role in disease pathobiology.

dpkjangir@gmail.com