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How Do Single Point Mutations Impact Protein Folding in Parkinson's Disease OLIVIA WISE-SCIRA, ANDREW ROQUE, LIANG XU, ORKID COSKUNER, University of Texas at San Antonio — Although the structures of the wild type (WT) and mutants (A53T, A30P, E46K) of α-synuclein (α-syn) proteins related to Parkinson's disease have been studied extensively using both experimental and theoretical tools, the relationships between the structural properties and thermodynamic preferences at a molecular level with dynamics are unknown. Such an understanding is required for accessing detailed knowledge regarding to the "early aggregation and monomer" hypothesis in Parkinson's disease. We investigated the impact of these single point mutations on the structures and conformational preferences of α-syn monomers in aqueous solution as well as the impact of the aqueous solution environment on the proteins. Obtained qualitative and quantitative results provide new insights into the structure-function relationships of these proteins and help us to understand the molecular mechanism hidden behind the "early aggregation and monomer" hypothesis. Our results show that the tertiary structure of the α-syn proteins varies significantly with dynamics, however, this variability is not easily reflected in the changes of the relative amounts of the secondary structural components. The obtained structures also demonstrate that a single point mutation can have a significant effect on protein folding. The structures of each of the WT, A53T, A30P, and E46K α-syn monomers differ from each other throughout and the presence of aqueous solution significantly impacts the α-syn protein structures.

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