

Impact of Single Amino Acid Substitutions in Parkinsonism Associated Deglycase-PARK7 and Their Association with Parkinson's Disease

ABSTRACT

Parkinsonism-associated deglycase-PARK7/DJ-1 (PARK7) is a multifunctional protein having significant roles in inflammatory and immune disorders and cell protection against oxidative stress. Mutations in PARK7 may result in the onset and progression of a few neurodegenerative disorders such as Parkinson's disease. This study has analyzed the non-synonymous single nucleotide polymorphisms (nsSNPs) resulting in single amino acid substitutions in PARK7 to explore its disease-causing variants and their structural dysfunctions. Initially, we retrieved the mutational dataset of PARK7 from the Ensemble database and performed detailed analyses using sequence-based and structure-based approaches. The pathogenicity of the PARK7 was then performed to distinguish the destabilizing/deleterious variants. Aggregation propensity, noncovalent interactions, packing density, and solvent accessible surface area analyses were carried out on the selected pathogenic mutations. The SODA study suggested that mutations in PARK7 result in aggregation, inducing disordered helix and altering the strand propensity. The effect of mutations alters the number of hydrogen bonds and hydrophobic interactions in PARK7, as calculated from the Arpeggio server. The study indicated that the alteration in the hydrophobic contacts and frustration of the protein could alter the stability of the missense variants of the PARK7, which might result in disease progression. This study provides a detailed understanding of the destabilizing effects of single amino acid substitutions in PARK7.