



On the oligomeric state of DJ-1 protein and its mutants associated with Parkinson disease. A combined computational and in vitro study.

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Streszczenie

Mutations in the DJ-1 protein are present in patients suffering from familial Parkinson disease. Here we use computational methods and biological assays to investigate the relationship between DJ-1 missense mutations and the protein oligomeric state. Molecular dynamics calculations suggest that: (i) the structure of DJ-1 wild type (WT) in aqueous solution, in both oxidized and reduced forms, is similar to the crystal structure of the reduced form; (ii) the Parkinson disease-causing M26I variant is structurally similar to the WT, consistent with the experimental evidence showing the protein is a dimer as WT; (iii) R98Q is structurally similar to the WT, consistent with the fact that this is a physiological variant; and (iv) the L166P monomer rapidly evolves toward a conformation significantly different from WT, suggesting a change in its ability to oligomerize. Our combined computational and experimental approach is next used to identify a mutant (R28A) that, in contrast to L166P, destabilizes the dimer subunit-subunit interface without significantly changing secondary structure elements.

Adres publiczny

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<https://www.asbmb.org/>

