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Genetic mutation and disordered protein structure

Orkid Coskuner

University of Texas, USA

Abstract

Intrinsically disordered proteins lack a stable structure and adopt many various conformations within a short time-scale. Genetic mutation impacts the structures and free energy landscapes of disordered proteins. The structure and function relationship definition in medicine and biology, which states that the 3-Dimensional structure of a protein defines its biological function captures native state proteins without serious limitations, however, intrinsically disordered proteins do not possess stable 3-Dimensional structures and yet they have well defined biological functions. For more than two decades, researchers from diverse fields have been trying to find a direct relationship between the structures and thermodynamic properties of intrinsically disordered proteins. Various tools have been developed without providing a direct relationship between the disordered protein structures and their thermodynamic properties, such as free energy. Most recently, we developed new theoretical strategies that relate genetic mutation directly to disordered protein structures and conformational free energy surfaces. In this talk, we will present these new strategies and their applications on genetic mutation and disordered proteins at the center of neurodegenerative diseases.