Molecular dynamics simulation and spectroscopic protein folding of human protein kinases: Implications in human health care

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ABSTRACT

Protein folding mechanisms have been extensively studied over the past few decades through both experimental and computational means. Better understanding of folding requires an accurate description of the transition state, for single domain, two-state proteins. Molecular dynamics (MD) simulations of protein unfolding at high temperature, harsh pH and denaturants with explicit water molecules have been widely used to characterize. Recent advances, however, have made combined experimental and computational studies of protein folding possible through the development of proteins that fold on the microsecond and even sub-microsecond timescale, and through advances in MD simulations allowing simulation of multiple microsecond folding trajectories. We have performed MD simulation of MAP/microtubule affinity-regulating kinase 4, Integrin linked kinase, Sphingosine kinase and Calcium/Calmodulin Dependent Protein Kinase IV. An excellent agreement was observed between results from biophysical and MD simulation studies. Our ongoing simulations on protein folding will attempt to directly link all-atom folding simulations with folding kinetics data. Through simulations of a variety of protein with different folding rates, we hope to gain a general understanding of factors driving protein folding.

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