A Molecular Dynamics Study of the Binary Complexes of APP, JIP1, and the Cargo Binding Domain of KLC

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Abstract

Mutations in the Amyloid Precursor Protein (APP) are responsible for the formation of Amyloid−β peptides. These peptides play a role in Alzheimer's and other dementia-related diseases. The cargo binding domain of the kinesin light chain 1 motor protein (KLC1) may be responsible for transporting APP either directly or via interaction with C-jun N-terminal kinase-interacting protein 1 (JIP1). However, to date there have been no direct experimental or computational assessment of such affinities at the atomistic level. We used molecular dynamics and free energy estimations to gauge the affinity for the binary complexes of KLC1, APP and JIP1. We find that all binary complexes (KLC1:APP, KLC1:JIP1 and APP:JIP1) contain conformations with favorable binding free energies. For KLC1-APP the inclusion of approximate entropies reduces the favorability. This is likely due to the flexibility of the 42-residue APP protein. In all cases we analyze atomistic/residue driving forces for favorable interactions.