Computational analysis of the interaction between kinesin light chain and amyloid precursor protein. Shah, Soleil. Holley, Dave, Miller III, Bill. Parish, Carol.

Interference within the binding between kinesin-1 light chain (KLC) and amyloid precursor protein (APP) has been implicated in a variety of diseases, including familial Alzheimer's. KLC serves to transport cargo, such as APP, across a microtubule; however, when this function is disrupted, APP releases and disrupts neuronal function. In this project, computational molecular dynamics (MD) was conducted on apo KLC, apo APP, and docked KLC-APP structures using the Amber MD package to understand the dynamics and interactions between the structures in atomistic detail. KLC remained stable in the apo state and helped to stabilize APP when docked. Preliminary per-residue free energy decomposition was utilized to determine the key residues involved in KLC-APP binding. MD was also conducted on an extended tetratricopeptide repeat (TPR) structure to observe fast-folding dynamics and produce the correct alpha-helical formation. TPR units, in tandem, form KLC's cargo-binding domain. Within 700 ns, TPR was able to fold to mostly resemble the consensus crystal structure (CTPR) to within an RMSD of 2.13 Å.