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Mutation Induced Conformational Change In CaMKII Peptide Alters Binding Affinity to CaM Through Alternate Binding Site JACOB EZERSKI, MARGARET CHEUNG, Univ of Houston — CaM forms distinct conformation states through modifications in its charge distribution upon binding to Ca^{2+} ions. The occurrence of protein structural change resulting from an altered charge distribution is paramount in the scheme of cellular signaling. Not only is charge induced structural change observed in CaM, it is also seen in an essential binding target: calmodulin-depended protein kinase II (CaMKII). In order to investigate the mechanism of selectivity in relation to changes in secondary structure, the CaM binding domain of CaMKII is isolated. Experimentally, charged residues of the CaMKII peptide are systematically mutated to alanine, resulting in altered binding kinetics between the peptide and the Ca^{2+} saturated state of CaM. We perform an all atom simulation of the wildtype (RRK) and mutated (AAA) CaMKII peptides and generate structures from the trajectory. We analyze RRK and AAA using DSSP and find significant structural differences due to the mutation. Structures from the RRK and AAA ensembles are then selected and docked onto the crystal structure of Ca^{2+} saturated CaM. We observe that RRK binds to CaM at the C-terminus, whereas the 3-residue mutation, AAA, shows increased patterns of binding to the N-terminus and linker regions of CaM. Due to the conformational change of the peptide ensemble from charged residue mutation, a distinct change in the binding site can be seen, which offers an explanation to experimentally observed changes in kinetic binding rates

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