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Solution Dynamics Studies for the Lck SH2 Domain Complexed with Peptide and Peptide-Free Forms

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It is well known that Src Homology 2(SH2) domain in many intracellular signal transduction proteins is very important. The domain has about 100 amino acid residues and bind phosphotyrosine-containing peptide with high affinity and specificity. Lck SH2 domain is a Src-like, lymphocyte-specific tyrosine kinase. An 11-residue phosphopeptide derived from the hamster polvoma middle-T antigen, EPQpYEEIPIYL, binds with an 1 nM dissociation constant to Lck SH2 domain. And it is known that the phosphotyrosine and isoleucine residues of the peptide are tightly bound by two well-defined pockets on Lck SH2 domain's surface. To investigate the conformational changes during complexation of SH2 domain with phosphopeptide we have performed the molecular dynamics simulation for Lck SH2 domain with peptide and peptide-free form at 300K in aqueous solution. More than 3000 water molecules were incorporated to solvate Lck SH2 domain and peptide. Periodic boundary condition has been applied in molecular dynamics simulation. Data analysis with the results of that simulation shows that the phosphopeptide makes primary interaction with the Lck SH2 domain at six central residues. The comparison of the complexed and uncomplexed SH2 domain structures in solution has revealed only relatively small change. But the hydrophilic and hydrophobic pockets in the protein surface show the conformational changes in spite of the small structural difference between the complex and peptide-free forms.