

Replica-Exchange Molecular Dynamics Simulations on the Phosphorylation of Phospholamban at Ser16

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Phospholamban is an integral membrane protein that works as an inhibitor of sarcoplasmic reticulum calcium pumping in the cardiac muscle. Its biological function is indeed important because its mutation causes dilated cardiomyopathy and heart failure. Here, we studied the structural effect of the phosphorylation of phospholamban at Ser16, using replica-exchange molecular dynamics (REMD) simulations. This method enables us to sample a wide conformational space of proteins, while avoiding trapping local energy minima. The simulations of the cytoplasmic domain of phospholamban show that its phosphorylation greatly disorders the helical structure due to the formation of multiple salt-bridges with the phosphate, whereas the helical structure remains stable when unphosphorylated. This observation agrees with recent NMR results and MD simulations of full-length phospholamban in a membrane environment.