Molecular dynamics simulations of the N-terminal domain of Hsp90 with nucleotides

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Heat Shock Protein 90 (Hsp90) is an ATPase-coupled molecular chaperone. Molecular chaperones are proteins which help client proteins fold. These proteins work to keep the client proteins folded and active in living cells. Heat shock proteins are molecular chaperones and have important functions to help client proteins fold and prevent them from the dangerous aggregation of immature proteins. Hsp90 is a specialized chaperone that has a more specific function in contrast to other Hsp molecules. Binding with ATP and hydrolysis of ATP to ADP are required for the normal function of Hsp90. The ATPase-coupled conformational rearrangement from the open to the closed state of Hsp90 dimer occurs [1]. In addition, Hsp90 is an interesting target for the therapy of virus infectious disease and cancer. For example, it is involved in the replication of influenza virus. Blocking the binding of ATP to Hsp90 causes the inhibition of ATPase activity. Then, the replication of viruses is inhibited. The formation of Hsp90-nucleotide complex is important for several functions. The purpose of our study is to investigate the molecular mechanisms of the formation of Hsp90-nucleotide complex.

We performed all-atom model molecular dynamics simulations of the N-terminal domain (NTD) of Hsp90 in complex with an ADP to elucidate the molecular mechanism of the ADP-binding. We investigated the relationships between the ADP-binding and hydrogen bonding networks.

References:

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