The interaction of NS5 protein with the human importin and exportin proteins

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Abstract

The Denv NS5 protein is well conserved among the 4 Denv serotypes, reflecting its vital role in the replication cycle of viral RNA. In order to replicate efficiently, viruses need to block host resistance mechanisms - which is achieved through viral proteins that control host machinery leading to viral replication and blocking eventual resistance mechanism, the NS5 protein blocks the cellular response for interacts with interferon proteins. Beyond of interferon proteins, the NS5 interacts directly with a large amount of proteins, including the proteins that import and export other to the cell nucleus. The mechanisms of NS5 interaction with that proteins is not know yet. To investigate this interactions, we use a methodology that uses the normal modes and docking approach. The approach uses Normal Modes to analysis is the approximation of the system's free energy dynamics to the Hooke Harmonic potential, which presents movements of the various protein regions around an energy minimum. Using VMOD protocol, were generated structures and using the lowest energy model can be investigated through the using of the concept of lower energy in an interaction between binding proteins and the use of the extended conformational selection model - thus representing the most likely conformational model for the docking between the two proteins. After that, large-scale tests of protein-protein interaction are performed. For these tests, proteins are treated as rigid bodies by making rotational and translational motions only, we provided conformational variations of each ligand and receptor obtained by normal modes analysis, as we selected the ligand hotspots through rigid docking, using the probability of the canonical ensemble. Stability tests and the adjustment of the interfaces were calculated by molecular dynamics. Through protein-protein docking experiment, we can find a possible hot-spot for docking between KPNB1-NS5 anb XPO1-NS5. This binding site is being confirmed through molecular dynamics, until stabilization of the system.

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