Study of dynamic properties and interactions of dimer effector domain of NS1 protein of Influenza A virus.

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The NS1 protein of influenza A virus is a homodimer, each monomer of 230 amino acids is formed by two domains, the RNA-binding domain (RBD) and the effector domain (ED), connected by a highly flexible unstructured region of ten amino acids («linker») [1]. NS1 binds to RNA (via its RBD domain) and different proteins (via its ED domain). Inhibition of ED domain interactions with other proteins would be a possible way to attenuate the virus replication. Crystallographic structures of full-length NS1 dimer revealed that it could dimerize into three distinct conformations (closed, semi-open and open form) depending on the orientation of the ED domains with respect to the RBD dimer. We studied the dynamic and interaction properties of dimer ED domains during molecular dynamics simulations. The three forms of the NS1 dimer were built by homology modeling based on H6N6 sequence and using full-length NS1 experimental structures as a template. These models served as initial structures to carry out the simulations. The effect of the linker and sequence variations between H6N6 strain and H5N1 strain (adopting the open form) on the stability of each model was highlighted. Our results are in good agreement with Carillo et al (2014) hypothesis [2]. Identification of ED's interface residues and stability assessment of ED-ED and RBD-ED contacts during molecular dynamics simulations helped to better understand the interaction properties of the ED domain.

[1] Aramini J.M. ; Montelione G.T. J. Biol. Chem 2011, 286 (29), 26050-60.
[2] Carillo B et al., J. Virology 2014, 88 (8), 4113-22.