Molecular Dynamics of the Viral IE1 Protein That Represents a Novel Protein Fold

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Recent studies have identified an intrinsic defense mechanism located in the nucleus of the cell that counteracts infection by cytomegalovirus. [1] One viral protein that targets this cellular immune response is immediate early 1 (IE1). The crystal structure of rhesus cytomegalovirus IE1 (rhIE1), which was recently determined by the group of Yves Muller, revealed a predominantly helical fold that exhibits no significant structural homology to any known structure. Interestingly, IE1 crystallizes in two slightly different dimeric forms, which exhibit small deviations of their monomer conformations and dimer interfaces. This indicates a certain degree of conformational plasticity of IE1, which was further investigated by molecular dynamics (MD) simulations.

All MD simulations were performed with AMBER/parm99SB force field in an octahedral box of explicit solvent. We simulated two dimer structures for 50 ns and three of the different monomers for 100 ns.

Furthermore we used MODELER 9.9 to create a homology model of HCMV IE1 (hIE1) with rhIE1 as a template. The modeled structure was then analyzed by MD in a similar fashion as rhIE1.

The monomers generally behaved much more flexible than the dimers. Interestingly, we detected a pronounced flexibility in adjacent parts of the helix-bundle resulting in a hinge like movement. Despite the low sequence identity of 24% between rhIE1 and hIE1, the same motions could also be detected in the simulations of modeled hIE1. We therefore assume that these hinge motions might be of biological relevance, e.g. for giving sufficient conformational plasticity for the interaction with different host proteins. In summary, we provide a first comprehensive insight into the dynamics and behavior of a novel protein fold.

[1] N. Tavalai, P. Papior, S. Rechter, T. Stamminger, *J. Virol.*, **2008**, *82*, 126-137.