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In Silico Design and Experimental Characterization of an Oligopeptide Targeting the Ebola Virus VP24 Protein

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Ebola virus is the etiologic agent of a hemorrhagic fever with a very high human fatality rate, ranging from 50% to near 90%. The virulence and high lethality of this virus are due to different factors in particular to its ability to inhibit both the innate immune response in the early stages of infection and the subsequent adaptive specific immune responses of the host organism. The Ebola viral Protein 24 (VP24) inhibits interferon signaling through its interaction with the human protein Karyopherin, thus impairing the immune response of the host against the infection and increasing its rate of diffusion into the organism and its lethality. This makes VP24 a potential pharmacological target, as the inhibition of its interaction with Karyopherin could reduce Ebola virulence. We carried out an atomic level study of the network of interactions between VP24 and Karyopherin using molecular dynamics and computational alanine scanning. Modeling the VP24–Karyopherin complex allowed us to identify the amino acid residues responsible for protein–protein binding and led to the identification of a nonapeptide with VP24 binding potential. Subsequently, the ability of this peptide to actually bind VP24 in solution has been assayed using Saturation Transfer Difference NMR and Circular Dichroism. Experimental and molecular modeling data concerning the VP24–peptide complex have been compared and putative peptide binding sites and modes will be discussed.

Biography:

Dr. Stefano Pieraccini is Assistant professor at the Chemistry department of Universita degli Studi di Milano. His research activity is focused on molecular modeling of biomolecules. In particular he is interested in the computational study of protein-protein interactions, using molecular dynamics and free energy calculations. In recent years, his group focused on the design and optimization of peptides and small molecules acting as protein-protein interactions inhibitors.