Different sequence motifs of the Herpesvirus Tip protein mediate binding specificity for STAT transcription factors

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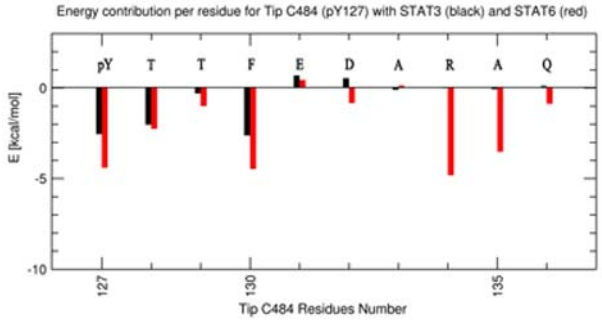
The transformation of human T-lymphocytes by *Herpesvirus saimiri* is a key mechanism of the viral infection that relies on the ability of the virus to manipulate the activity of T-cell signalling molecules. For this purpose, *Herpesvirus saimiri* uses a tyrosine kinase interacting protein (Tip) that is capable to activate several transcription factors belonging to the STAT family (‘signal transducers and activators of transcription). Tip phosphorylation at a tyrosine residue is required for the binding of STAT SH2 domain, the tyrosine phosphorylation of STAT itself, and the induction of STAT-dependent transcription. [1] Tip proteins possess three strictly conserved tyrosine residues, of which two (Tyr114, Tyr127) have been shown experimentally to become phosphorylated. While Tyr114-phosphorylation is known to be required for STAT1 binding, the role of the different phosphorylation sites for STAT6 interaction is not yet fully understood
In this study, the interaction of the tyrosine Tyr114- and Tyr127-phosphorylated peptides of Tip with the regulatory SH2 domain of STAT1 and STAT6 was investigated by computational techniques (Molecular Dynamics Simulations and MM/GBSA analysis) to address their binding specificity for different STAT members.



[1] D. A. Hartley, G. M. Cooper, . *Biol. Chem.*, **2000**, *275*, 16925-16932.