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Herpesvirus *saimiri* Tip Induces Phosphorylation but not Nuclear Translocation of STAT6 in T cells

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Herpesvirus persists in its host by entering a latent state, periodically reactivating to produce infectious viral particles. Some of the herpesviruses have also been known to be related to cancers. Herpesvirus *saimiri* (HVS), an oncogenic monkey herpesvirus, persists in the T lymphocytes of its natural host, the squirrel monkey, without any apparent disease symptoms, but infection of other species of New World and Old World primates results in fulminant T cell lymphomas. Two viral oncoproteins, Saimiri Transforming Protein and Tyrosine kinase-interacting protein (Tip), are required for T cell transformation. It has been known that Tip may also play some role in viral persistency within T cells by inhibiting the activation of the host cells upon antigenic stimulation. Recently, we found that Tip could induce phosphorylation of STAT6 as well as STAT3. Interestingly, the phosphorylated STAT6 were colocalized with vesicles containing Tip within T cells but not detected in nucleus. Stimulation of T cells expressing Tip with IL-4, which could activate STAT6 signaling, did not significantly affect the interaction of Tip with phosphorylated STAT6, even though nuclear translocation of phospho-STAT6 was increased. Our current hypothesis is that Tip-mediated phosphorylation of STAT6 and its retention in Tip containing vesicles might be involved in viral pathogenesis since several recent reports have suggested that constitutively active STAT6 could contribute lymphoprolierative disorder. To prove this, we are characterizing the molecular interaction of Tip and STAT6 and their potential role in T cell transformation.

Keywords: Herpesvirus saimiri, Tip, STAT6, T cell