# HTLV-1 Tax Protein Suppresses Type I Interferon Production by Inhibiting IRF3 Phosphorylation

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**Background/Objective**
Human T-cell lymphotropic virus type I (HTLV-1) is an oncogenic virus etiologic to adult T-cell leukemia (ALT). During HTLV-1 infection, the oncogenic viral protein Tax is expressed to suppress host antiviral response. It represses the expression of interferon-stimulated genes (ISGs) by stabilizing the negative regulator SOCS1. However, how Tax affects the more upstream Type-I interferon induction pathway remains only partially understood.

**Method**
Luciferase reporter assay was performed to assess transcriptional activation. Expression levels of genes were monitored by quantitative RT-PCR. Co-immunoprecipitation was used to study protein-protein interaction. In vitro kinase assay was conducted to confirm kinase activity.

**Result**
Tax potently inhibits interferon-$\beta$ (IFN$\beta$) production by dephosphorylating IRF3, which is an essential component of the transcription factor complex for IFN$\beta$. HTLV-1 transformed ALT cells expressing Tax completely abrogated IFN$\beta$ transcription upon Sendai virus infection. Overexpression of Tax alone was sufficient to inhibit IFN$\beta$ production induced by RIG-I and PIG-I+PACT or TBK1, but not by IRF3-5D, a dominant active form of IRF3 mimicking the phosphorylated IRF3. Reciprocal co-immunoprecipitation study using HTLV-1 transformed ALT cells revealed that Tax associated with endogenous TBK1, the kinase that phosphorylates IRF3. In vitro kinase assay also showed that recombinant Tax protein inhibited phosphorylation of IRF3 mediated by TBK1 in dose-dependent manner.

**Conclusion**
HTLV-1 Tax represses IFN$\beta$ production by physically associating with TBK1, inhibiting it from phosphorylating IRF3.

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