# Regulation of key lymphotropic factors by the transcription factor Ets-2 in T cell lines modeling uninfected and virus-infected T cells

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Ets-2 is a transcriptional regulator associated with cell differentiation. Our recent work showed that Ets-2 downregulates the expression of cytokine genes and HIV-1 in resting but not in activated T cells. In this work, we investigated Ets-2 role in regulating the expression of NFAT2, NF-κB/p65, c-Jun and c-Fos lymphotropic factors, which play critical role in T cell activation and differentiation, and CDK10 kinase, which controls Ets-2 degradation. In-silico analysis revealed putative Ets-2 binding sites at the NFAT2, c-Jun and c-Fos promoters. T cell lines Jurkat (modeling T cell signaling/activation) and H938 (containing full HIV-1 LTR) were transfected with increasing amounts of an Ets-2 overexpressing vector in the presence/absence of mitogens. mRNA levels were determined by qPCR and protein levels by Western immunoblotting. In unstimulated Jurkat cells, Ets-2 overexpression resulted in upregulation of NFAT2 and c-Jun mRNA and protein, increase in c-Fos mRNA and NF-κB/p65 protein, and downregulation of CDK10 mRNA and protein. In unstimulated H938 cells, Ets-2 increased NFAT2, c-Jun, and CDK10 mRNA and protein and increased NF-κB/p65 protein. In stimulated Jurkat cells, Ets-2 increased NFAT2, c-Jun, and c-Fos mRNA and protein and decreased CDK10 mRNA and protein. In stimulated H938 cells, Ets-2 increased NFAT2, c-Jun, and c-Fos protein and decreased CDK10 protein. In summary, Ets-2 upregulates key lymphotropic factors expression, either through its physical interaction with gene promoters or through its involvement in signaling pathways that have a direct effect on their expression. In Jurkat cells, Ets-2 downregulates CDK10 expression to its advantage. Although Ets-2 downregulates CDK10 expression in stimulated H938 cells, CDK10 is upregulated in unstimulated cells, accelerating its degradation; this may lead to disruption of HIV latency in resting virus-infected T cells.
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