

ALX OVEREXPRESSION INHIBITS TCR/CD28
TRANSCRIPTIONAL ACTIVATION OF THE RE/AP COMPOSITE
ELEMENT

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T cell activation requires two signals: specific recognition of antigen through the T cell receptor (TCR) and a costimulatory signal, provided primarily by CD28 in naïve T cells. At the transcriptional level, TCR and CD28 signals synergize to upregulate the IL-2 promoter through the RE/AP composite element. Recently, we cloned a novel gene, containing one SH2 domain, three conserved polyproline motifs and two conserved potential sites for tyrosine phosphorylation and no apparent catalytic domains. Expression of this gene is limited to spleen and thymus. We have named this gene "ALX", Adaptor in Lymphocytes of Unknown Function ("X"). ALX overexpression in Jurkat T cells results in inhibition of RE/AP activation after TCR/CD28 stimulation. Interestingly, ALX overexpression has minimal effect on the activation of either an NFAT or AP-1 reporter after TCR stimulation. We have mutated the six conserved motifs in ALX, and found that the SH2 domain is required for RE/AP inhibition. Therefore, it appears that ALX may function downstream of CD28 costimulation during T cell activation.

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