

## **ALX negatively regulates T cell activation**

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Signals originating from the T cell receptor and CD28 synergize to produce optimal activation of naïve T cells. Previously, we cloned a novel adaptor, ALX (Adaptor in Lymphocytes of unknown function, X). In vitro studies suggested that ALX may negatively regulate TCR/CD28-mediated IL-2 promoter activation. To gain insight into the physiological role of this molecule, ALX-deficient mice were generated. T and B cell development proceeded normally. In vitro, ALX-deficient splenocytes produced more interleukin-2 (IL-2) in response to CD3 and CD28 stimulation. Correspondingly, increased proliferation was also observed. Examination of signaling pathways downstream of TCR/CD28 demonstrated constitutive p38 activation in ALX-deficient splenocytes. To examine the effect of the loss of ALX on immune system function in vivo, responses to Staphylococcal enterotoxin B (SEB), to nitrophenyl-keyhole limpet hemocyanin (NP-KLH), and to ovalbumin (OVA) were assessed. SEB-mediated V $\beta$ 8<sup>+</sup> T cell deletion in ALX-deficient mice, as well as T-dependent B cell responses to NP-KLH immunization, did not differ significantly from wild type. However, T cell proliferation to OVA after in vivo priming was significantly higher in the absence of ALX. Taken together, our results demonstrate that ALX negatively regulates T cell activation.

Supported by NIH RO1 AI054974 to V.S.S.