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Poster Abstract

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Regulation of gene expression during the early polarization of Th1 and Th2 cells

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T helper cell subtypes (Th1 and Th2) are involved in many immune mediated diseases. To better understand the pathogenesis of these diseases, it is essential to know the molecular mechanisms driving the Th1 and Th2 polarization. The detailed model of the process and especially the earliest events, which determine the fate of naïve precursor cell are largely unknown. We have studied the regulation of gene expression during the early Th1 and Th2 polarization (Chen et al, 2003, Lund et al. 2003). In addition to IL-12 and IL-4, the effects of TGF β on the Th1 and Th2 differentiation were studied. TGF β is a cytokine secreted by regulatory T cells and inhibits the differentiation process. In addition to genes previously implicated in the process, we have identified over 100 genes with various known and unknown functions not previously associated with Th1 and Th2 polarization. Importantly, a subset of genes was coregulated by IL-12 or IL-4 and TGF β . Moreover, IL-12 and STAT4 signaling was studied further by analysing the gene expression profiles of wild type and STAT4-knockout T helper cells during the early Th1 differentiation. As a result, 20 genes regulated by IL-12 and STAT4 were identified. In conclusion, our studies have resulted in identification of a number of novel candidates whose functional role in lymphocyte Th subset differentiation is being further elucidated.

References:

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