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Oral presentation

Transcriptional regulation of Th2 differentiation

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Naïve CD4 T cells have a series of fates open to them; differentiation to Th2 cells depends on the concerted action of three transcription factors, GATA-3, STAT5 and Gfi-1, and displays striking positive reinforcement. The earliest events in Th2 differentiation are T cell receptor driven induction of GATA-3 and of IL-2, the latter activating STAT5. GATA-3 and STAT-5, acting together, lead to early transcription of IL-4. Endogenous IL-4, acting through IL-4Rα and STAT6 strikingly upregulate GATA-3 and IL-4, leading to commitment of the cell to high rate IL-4 production and to the Th2 phenotype. GATA-3 and STAT5 target distinct sites within the Il4 gene, resulting in accessibility and thus the two transcription factors work in concert to activate the gene. Gfi-1 enhances the cytokine driven out-growth of Th2 cells and selects cells expressing the highest amounts of GATA-3. Thus, the interaction of the three transcription factors leads both to Th2 fate determination and selective outgrowth of differentiated Th2 cells and are thus responsible for a robust differentiation process resulting in the appearance of CD4 T cells capable of producing IL-4 and its related cytokines.