Retrovirology

Oral presentation

GATA3 and STAT5 – Critical Inducers of the Th2 Fate

Jinfang Zhu, Hidehiro Yamane and William E Paul*‡

Address: Laboratory of Immunology, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, MD, USA 20892

Email: William E Paul* - wepaul@nih.gov

* Corresponding author ‡Presenting author

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GATA3 has been implicated as a key factor in commitment of CD4 T cells to the Th2 phenotype. Naïve CD4 T cells cultured without exogenous cytokines induce GATA3 and IL-4 transcription only when stimulated with low concentrations of cognate peptide in the presence of IL-2. Naïve CD4 T cells from mice with a conditional deletion of *Gata3* fail to induce IL-4 in response to TCR engagement as do cells cultured in the presence of anti-IL-2. High concentration inhibition of GATA3 and IL-4 expression and of Stat5 signaling is rescued by MEK inhibitors implying that inhibition is mediated through *erk* action. Infection of cells cultured under Thnull conditions with retroviruses containing GATA3 and constitutively active Stat5a induce a Th2 phenotype and result in full accessibility of the *Il4* gene. Further, ChIP analyses reveals that in Th2 cells, Stat5a is bound to DNase I hypersensitive sites in the second exon of the *Il4* gene. Thus, both GATA3 and STAT5 are key factors in "opening" the *Il4* gene and in inducing the Th2 phenotype. Furthermore, GATA3 proved to be important in Th2 growth. *In vivo* deletion of Gata3 using OX40-Cre eliminated Th2 responses and allowed the development of IFNg-producing cells in mice infected with *Nippostrongylus brasiliensis*. Thus, GATA3 serves three functions in Th2 biology; it induces the Th2 fate, represses the Th1 fate and it promotes selective outgrowth of Th2 cells.