A34 NFAT2 AND STAT3 CONTROL TYPE 2 CYTOKINES IN CD5 B CELLS

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Purpose Autoimmunity and inflammation are controlled in part by regulatory B cells expressing interleukin 10 (IL-10). Since, one of the characteristic of CD5 B cells lies in their capacity to produce IL-10, the aim of the subject was to characterise the transcription factors (TF) involved.

Method To address this question stably transfected CD5 B cells expressing the cell surface isoform, CD5-E1A, or the intracellular isoform, CD5-E1B, were generated and compared to normal B cells (CD5 blood B cells, CD5 cord blood B cells and CD5 from B chronic lymphocytic leukaemia), T cells and CD5 transfected HepG2 cells.

Results Based on the observation that NFAT2 is constitutively present in the nucleus of CD5 B cells and that STAT3 is phosphorylated in its S727, we have tested the implication of these two TFs on the expression of IL-10. First, using specific inhibitors-like cyclosporine A (NFATs inhibitor) and AG490 (Jak-2/STATs inhibitor) that abrogate IL-10 expression in CD5 B cells. Second, using a chromatin immunoprecipitation assay to reveal that both TFs bind the IL-10 enhancer in CD5 B cells. Interestingly, NFAT2/STAT3 activation is not restricted to IL-10 since we observed that IL-5 and IL-13 promoters recruits NFAT2/STAT3 and express both transcripts in CD5 B cells. Finally, such effect is restricted to CD5 B cells because it was not observed in T cells and CD5-transfected HepG2 cells.

Conclusion Results indicate that constitutive calcineurine/NFAT2 and Jak2/STAT3 pathways contribute to cytokine type 2 expression in CD5 B cells. This observation provides new directions to polarise the immune system.