downregulation of RORc mRNA expression. Finally, exogenous IL-2 restores IL-2R α expression on SKG T cells.

Conclusions These data indicate that a state of relative IL-2 deficiency is characteristic of effector T cells with impaired antigen TCR signalling. Lack of IL-2 promotes differentiation of Th17 cells, at the expense of Th2 cells, through failure downregulate expression of the Th17 master transcription factor, RORc.

A114 ARTHRITOGENIC SKG T CELLS ARE IL-2 DEFICIENT AND DEMONSTRATE DISTINCT PATTERNS OF TH CELL DIFFERENTIATION; REVERSAL OF THE TH17 PHENOTYPE BY IL-2

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Background and objectives Emerging data suggest that a growing number of allelic variants in immunologically important genes modify T cell antigen receptor (TCR) signaling thresholds in ways that predispose individuals to autoimmune inflammatory arthritis, including rheumatoid arthritis (RA). SKG mice carry a loss of function spontaneous mutation in the TCR proximal protein tyrosine kinase ZAP-70, and develop a T cell dependent autoimmune inflammatory arthritis resembling RA. The authors set out to explore the mechanisms whereby SKG T cells promote disease, focusing on pathways of T cell activation and differentiation.

Materials and methods To study antigenic peptide specific responses, SKG mice, on the Balb/c background were crossed to the HNT-TCR transgenic mouse, in which CD4 T cells are specific for a haemagglutinin specific peptide, to generate SKG^{+/+}HNT-TCR⁺ mice. HNT-TCR single transgenic mice were used as controls. Th cell differentiation was studied by stimulating naïve lymph node derived CD4 T cells with specific peptide and cultured for 7–9d prior to restimulation with antigen. Proliferation was measured by CFSE dye dilution and cytokine expression was determined by the cytokine bead array method, and transcription factor expression measured by RT-PCR. Interleukin (IL)-2R signalling was evaluated by p-STAT5 immunoblotting.

Results SKG T cells proliferate poorly and produce very low levels of IL-2, compared to control T cells. Differentiation of naïve SKG T cells in vitro leads to the preferential generation of cells in which IL-17 is upregulated. Levels of tumour necrosis factor, IL-6 and IFN γ are unchanged, while IL-4 and IL-10 production was substantially reduced. Consistently, levels of T-bet in differentiating SKG T cells are unchanged, expression of GATA-3 is reduced and that of RORc is substantially upregulated, when compared to HNT-TCR single transgenic mice. Restoration of IL-2 production during differentiation of naïve SKG T cells leads to suppression of IL-17 secretion and

Corrections

Oli Smonezi, Alex Annenkov, Tharsana Tharmalingam, *et al.* Arthritogenic SKG T cells are il-2 deficient and demonstrate distinct patterns of Th cell differentiation; reversal of the th17 phenotype by il-2. *Ann Rheum Dis* 2011;**70**(Suppl 2):A1–A94. The name of the author Oli Somenzi was incorrectly published as Oli Smonezi.

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