A173 **INTERLEUKIN (IL)23 PROMOTES TH17 DIFFERENTIATION BY INHIBITING T-BET AND FOXP3 AND IS REQUIRED FOR IL22 BUT NOT IL21 IN AUTOIMMUNE EXPERIMENTAL ARTHRITIS**

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Objective To unravel the role of interleukin 23 (IL23) in subgroup polarisation of IL17α and/or interferon γ (IFNγ) T cells in the prone autoimmune DBA-1 mice with and without collagen-induced arthritis.

Methods CD4 T cells were isolated using the MACS system from the spleen of naive and type II collagen (CII) immunised DBA-1 mice. These CD4 T cells were stimulated in vitro under Th0, Th1 or different Th17 conditions. Intracellular staining for IL17A and IFNγ was evaluated by flow cytometry. In addition, Th17 cytokines and T-helper-specific transcription factors were analysed by ELISA and/or Q-PCR.

Results In CD4 T cells from naive DBA-1 mice, IL23 alone hardly induced RORγt, Th17 polarisation and Th17 cytokines but inhibited T-bet expression. In contrast, transforming growth factor (TGFβ)/IL6 was a potent inducer of RORγt, RORα, IL17α, IL17F, IL21 and FoxP3 in these cells. IL23 in contrast to TGFβ/IL6 was critical for the induction of IL22 in CD4 T cells from both naive and CII-immunised DBA-1 mice. In line with these findings, IL23 was more pronounced in inducing the IL17A IFNγ subset in CD4 T cells from CII-immunised mice. However, under naive conditions, IL23 significantly increased the TGFβ/IL6-induced Th17 polarisation including elevated IL17α and IL17F levels and decreased T-bet and FoxP3 expression. Of note, the IL23-induced increase in IL17A and IL17F was prevented in T-bet-deficient mice.

Conclusion IL23 promotes Th17 differentiation by inhibiting T-bet and FoxP3 and is required for elevation of IL22 but not IL21 in autoimmune arthritis. These data indicate different mechanisms for IL23 and TGFβ/IL6 at the transcription factor level during Th17 differentiation in autoimmune experimental arthritis.