A136 IMPAIRED B CELL IMMUNITY IN IL-22 KNOCK-OUT MICE IN COLLAGEN INDUCED ARTHRITIS

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Background The role of IL-22, a cytokine produced by Th17 cells, in autoimmunity is not fully understood. Previous research has shown that IL-22 is important in the development of collagen induced arthritis (CIA). However, the mechanism behind the apparent protection in IL-22 knock-out mice against CIA remains unclear.

Objective To investigate the mechanisms by which IL-22 knock-out mice are protected against collagen induced arthritis.

Materials and methods For CIA, IL-22 knock-out and wild type mice were immunised with chicken collagen type II and complete Freud's adjuvant (CFA) and boosted 21 days later. Antigen specific serum IgG levels were measured by ELISA. Mice were sacrificed 50 days after immunisation. Splenocytes were analysed by flow cytometry and immunohistochemistry.

Functional assays were performed with splenic Th17 cells sorted from mice ten days after immunisation. For antigen induced arthritis (AIA), mice were immunised with methylated bovine serum albumin (mBSA) and CFA and triggered seven days later by intra-articular mBSA injection.

Results In IL-22 knock-out mice, the severity, but not the incidence, of CIA was lower compared to wild type controls. This prompted us to study the pathogenicity of Th17 cells from these mice. Synovial fibroblasts produced higher levels of IL-6 when co-cultured with Th17 cells from IL-22 knock-out mice compared to wild type Th17 cells. To study the pathogenicity in vivo, we made use of the Th17 mediated AIA model. IL-22 knock-out mice developed AIA similarly to wild type controls, showing that Th17 cells without IL-22 function normally in vivo. As CIA is strongly driven by B cells and immune complexes, we investigated whether B cell immunity is normal in IL-22 knock-out mice. Antigen specific serum IgG2a levels were significantly lower in IL-22 knock-out mice at early onset of disease. We observed no significant differences in splenic B cell numbers or activation**.** However, spleens from IL-22 knock-out mice show no or very small germinal centers and fewer IgG2a plasma cells compared to wild type controls.

Discussion Here we show that lack of IL-22 production affects B cell immunity in CIA. However, Th17 cells in IL-22 knock-out mice function normally in vitro and in vivo, indicating that lack of IL-22 production does not affect the pathogenicity of Th17 cells. Importantly, germinal center formation, plasma cell formation and IgG2a antibody production are lower in IL-22 knock-out mice in CIA, suggesting that IL-22 has a role in further differentiation of B cells in autoimmunity.