9 MODULATION OF IL-17 PRODUCING CELLS IN ESTROGEN-MEDIATED INHIBITION OF EXPERIMENTAL ARTHRITIS

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Background and objectives Endogenous hormones play a role in regulating the development of autoimmune diseases. In rheumatoid arthritis (RA) estrogen treatment alleviates the disease, however due to severe side effects it is not a suitable therapy. It is important to clarify the effects of estrogen on the immune system to be able to take advantage of its beneficial effects in RA. The proinflammatory cytokine IL-17 has emerged as a key player in driving autoimmunity. The aim of this study was to investigate the effects of estrogen on IL-17 producing cells (Th17 and $\gamma\delta TCR^{+}IL\text{-}17^{+}$) in experimental arthritis.

Material and methods Ovariectomised DBA/1 mice with collagen-induced arthritis (CIA) underwent treatment with 17β-estradiol (E2) or placebo. Experiments were terminated at several time points during the disease development and IL-17 producing cells were analysed with flow cytometry.

Results As expected, E2 treated mice displayed less severe and lower frequency of arthritis compared to the placebo group. Surprisingly, E2 treatment increased the frequency of IL-17 producing cells in draining lymph nodes of mice with CIA. However, E2 had the opposite effect in joints and decreased the number of IL-17-producing cells compared to placebo. Fewer IL-17-producing cells in joints of E2 treated mice were accompanied with a reduction in the number of neutrophils. CCR6 is a chemokine receptor that is important for the migration of cells into the joints. Interestingly, treatment with E2 specifically decreased the frequency of $CCR6^{+}$ IL-17 producing cells in joints.

Conclusions E2 treatment ameliorates arthritis and one mechanism might be by regulating IL-17 producing cells (Th17 and $\gamma\delta TCR^{+}IL\text{-}17^{+}$). Mice receiving E2 treatment displayed an increase of IL-17 producing cells in lymph nodes but a decrease of IL-17 producing cells in joints, compared to placebo. A possible explanation for this phenomenon is that E2 affects the ability of the IL-17 producing cells to migrate from lymph nodes to the blood and into the site of inflammation, the joint. This hypothesis is strengthened by the fact that treatment with E2 decreased the frequency of $CCR6^{+}$ IL-17 producing cells in the joint, however further investigations are needed to verify this theory.