

A118 LACK OF IL-17RA SIGNALLING PREVENTS AUTOIMMUNE INFLAMMATION OF THE JOINT AND GIVE RISE TO A TH2-LIKE PHENOTYPE IN COLLAGEN-INDUCED ARTHRITIS

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Interleukin (IL)-17A plays an important role in collagen-induced arthritis (CIA). On the other hand, CIA developed normally in IL-17F deficient mice. This could be due to IL-17A that is still expressed in these mice. It has been shown that around 20% of the IL-17A deficient mice still develop marked collagen-induced arthritis with a somewhat lower severity than the control littermates. Spontaneous arthritis development in the IL-17A deficient mice could not be completely prevented in double IL-17A/IL-17F deficient mice. However, it is still not fully clear how important the role of the IL-17A and IL-17F signalling is in the development of autoimmune collagen-induced arthritis.

Here the authors examined the role of the IL-17RA signaling in the development of CIA using IL-17RA deficient (IL-17RA^{-/-}) mice that can not signal for IL-17A and IL-17F. These mice were compared to control mice and the CIA resistant IL-23p19 deficient (IL-23p19^{-/-}) mice.

CII-immunised control mice developed CIA from day 24 onwards with an incidence between 40% and 60%. As expected, the IL-23p19^{-/-} mice did not develop CIA. Interestingly, the IL-17RA^{-/-} mice were completely protected and did not develop CIA even after a third CII/CFA injection. In contrast to the low percentage of IL-17⁺ CD4⁺ T cells in the IL-23p19^{-/-} mice, there was a significant increase in the percentage of these cells in the IL-17RA^{-/-} group compared to the control group at day 69. No significant difference was found in the percentage of IFN- γ ⁺ CD4⁺ T cells between all three groups. Interestingly and in contrast to the IL-23p19 knockout mice, the IL-17RA deficient mice showed a Th2-like phenotype in splenic CD4 T cells at day 69. No difference was noted for FoxP3 expression in the splenic CD4 T cells between the three different mouse groups. Moreover, the CII-specific IgG2a levels in the sera of IL-17RA^{-/-} was significantly lower compared to the control group at day 20 and lower although not statistically significant at day 69. At this latter time point, CII-specific IgG1 levels in the sera of IL-17RA^{-/-} was increased although not statistically significant compared to the control.

These data revealed a critical role for the IL-17RA signaling in the development of autoimmune inflammation of the joint. Moreover, these data show a Th2-like phenotype in IL-17RA^{-/-} mice immunised with CII, suggesting that IL-17 receptor signaling is involved in the suppression of Th2 cytokines in autoimmune collagen arthritis.