Rheumatoid arthritis - etiology, pathogenesis and animal models

**AB0109**

**SYSTEMIC OVEREXPRESSION OF INTERLEUKIN-22 INDUCES EXPRESSION OF THE NEGATIVE IMMUNE-REGULATOR SOCS3 AND POTENTLY REDUCES COLLAGEN-INDUCED ARTHRITIS IN MICE**

Joyce Aarts, Debbie Roeleveld, Monique Helsen, Birgitle Wallgren, Elly Vitters, Peter van Lent, Fons van de Loo, Wim van den Berg, Peter van der Kraan, Marie Koenders. RIMLS, Experimental rheumatology, Nijmegen, Netherlands

**Background:** High interleukin-22 (IL-22) levels are detected in serum and synovial fluid of rheumatoid arthritis (RA) patients. The increased IL-22 serum levels in RA patients correlated positively with multiple clinical disease parameters like disease activity score (DAS)28 and serum levels of rheumatoid factor. The role of IL-22 in autoimmunity and inflammation appears to be greatly contradictory, being both pro- and anti-inflammatory. Especially the anti-inflammatory properties of IL-22 are not well understood.

**Objectives:** We aimed to investigate the anti-inflammatory and immune-suppressive effect of IL-22 during experimental arthritis.

**Methods:** Collagen-induced arthritis was induced in DBA1 mice by immunization and booster with bovine collagen type II (CII). After booster, but before arthritis onset, IL-22 was overexpressed either locally or systemically using an adenoviral construct (AdIL-22) or Luciferase as control (AdLuc). 1x10⁷ plaque-forming units (PFU) of the adenoviruses were injected intra-articularly for local overexpression, or 3x10⁸ PFU was injected intravenously for systemic overexpression in immunized mice, and mice were sacrificed 10 days later. Macroscopic scoring and histological analysis was performed, and mRNA expression and protein production of various pro- and anti-inflammatory mediators was determined in synovial tissue, spleen, and serum.

**Results:** Local overexpression of IL-22 by injection of AdIL-22 in the knee joint of CII-immunized mice resulted in an unaltered arthritis incidence and severity as compared to the control virus AdLuc. Accordingly, no changes in mRNA expression or protein production were observed in CIA mice locally overexpressing IL-22. In contrast, systemic overexpression of IL-22 potently reduced disease incidence and severity, which was also confirmed by histological analysis. Systemic levels of IL-1β, IL-17, GM-CSF and MCP1 were unaltered in mice overexpressing IL-22 systemically. However, these mice showed significantly lower serum levels of IFNγ, TNFα, MIP1α, and IL-10. Interestingly, the significantly enhanced splenic SOCS3 expression was found to negatively correlate to serum TNFα and MIP1α levels, which is in line with our hypothesis that the observed reduction in the cytokine levels is mediated in a SOCS3-dependent manner.

**Conclusion:** With this study, we revealed clear anti-inflammatory effects of IL-22 overexpression during collagen-induced arthritis, which are completely dependent on the systemic route of administration. Additionally, we were the first to show that this protective effect of IL-22 during experimental arthritis is likely orchestrated via up-regulation of the negative regulator SOCS3.

**Disclosure of Interests:** None declared