bone destruction and cartilage damage were also significantly diminished when compared to IL-6$^{-/-}$hTNFtg mice. However, by comparing IL-1$^{-/-}$IL-6$^{-/-}$hTNFtg mice with IL-1$^{-/-}$hTNFtg mice the authors found a similar reduction on synovial inflammation, as well as subchondral bone erosions and articular cartilage destruction.

Conclusion The phenotype of IL-1$^{-/-}$IL-6$^{-/-}$hTNFtg mice does not differ from IL-1$^{-/-}$hTNFtg animals indicating no synergistic effects when IL-1 and IL-6 is simultaneously blocked in TNF mediated arthritis.

A168 COMBINED DEPLETION OF INTERLEUKIN 1 AND INTERLEUKIN 6 DOES NOT EXCEED SINGLE DEPLETION OF INTERLEUKIN 1 IN TNF MEDIATED ARTHRITIS

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Background Previous studies demonstrated a regulatory role of interleukin 1 (IL-1) in inflammatory cartilage damage and bone destruction in human tumour necrosis factor transgenic (hTNFtg) mice, an animal model for rheumatoid arthritis. Moreover, blocking of IL-6 has been shown to reduce local bone erosions in this model. Therefore the authors wanted to investigate the effect of a combined depletion of IL-1 and IL-6 on the development and severity of inflammatory, erosive arthritis.

Methods The authors first crossed IL-1α and ß deficient (IL-1$^{-/-}$) mice with IL-6$^{-/-}$ mice to generate IL-1$^{-/-}$IL-6$^{-/-}$ double knockout mice. The authors next intercrossed these animals with arthritogenic hTNFtg mice to receive IL-1$^{-/-}$IL-6$^{-/-}$hTNFtg mice. The authors weekly assessed clinical signs of arthritis in hTNFtg, IL-1$^{-/-}$hTNFtg mice, IL-6$^{-/-}$hTNFtg mice and IL-1$^{-/-}$IL-6$^{-/-}$hTNFtg mice starting from week 4 after birth until week 16. The authors stained decalcified paw sections from all four genotypes with H&E to determine the amount of inflammatory synovial pannus formation, with tartrate-resistant acid phosphatase (TRAP) to evaluate the number of synovial osteoclasts and the occurrence of subchondral bone erosions, with toluidine-blue to assess articular cartilage damage. Quantitative analysis of histopathological changes were performed using the Osteomeasure Software System.

Results The authors found a significant reduction in the clinical signs of arthritis, indicated by an increase of paw swelling and a decrease in grip strength, in IL-1$^{-/-}$IL-6$^{-/-}$hTNFtg mice when compared to their hTNFtg littermates. In line with these findings the authors observed a significant decrease in synovial inflammation in IL-1$^{-/-}$IL-6$^{-/-}$hTNFtg mice when compared to hTNFtg animals. Moreover, the number of synovial TRAP+ osteoclasts was markedly diminished in IL-1$^{-/-}$IL-6$^{-/-}$hTNFtg mice and reduced osteoclast formation was accompanied by significantly less subchondral bone erosions. Additionally, the authors found a conserved articular cartilage structure showing almost no cartilage degradation in IL-1$^{-/-}$IL-6$^{-/-}$hTNFtg mice compared to their hTNFtg littermates. In IL-1$^{-/-}$IL-6$^{-/-}$hTNFtg mice clinical, as well as, histological signs of disease, including joint inflammation,