The role of CD11c+ dendritic cells in inflammatory Arthritis

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Backround. Dendritic cells (DCs) play an important role in bridging the innate and the adaptive immune response by serving as antigen presenting cells and are therefore implicated in the initiation of chronic autoimmune diseases, including rheumatoid arthritis.
Using the K/BxN serum transfer arthritis, a model of human rheumatoid arthritis, which depends only on the innate immune system, we investigated the innate role role of dendritic cells in inflammatory arthritis.

Methods. KBxN serum transfer arthritis was induced in CD11c-diphteria toxin receptor (DTR) transgenic mice, which express the human diphtheria-toxin receptor under the CD11c promoter. This allows for specific depletion of CD11c+ cells by administration of diphtheria toxin (DT). In addition CD11c DTR mice were crossed into hTNFtg animals and either PBS or DT during week 6 and 8. DT or PBS was given in KBxN on day -1, 3, 6 and 9. The severity of arthritis was determined clinically and histologically. Wild type animals, which also received DT served as a control.

Results. We show that Cd11+ cells are present in significant numbers in the synovia of K/BxN and TNF driven arthritis. Both myeloid dendritic subsets, CD8+ CD11c+ and CD11b+ CD11c+, can be found in similar amounts in synovial tissue. Clinical scores of arthritis showed that CD11c-DTR transgenic mice that received DT had significantly reduced paw swelling and loss of grip strength compared to PBS treated animals. In contrast, wild type animals receiving DT showed identical clinical signs of arthritis as PBS treated animals, excluding unspecific effects of DT in mice. Histological analysis found reduced inflammation after the depletion of CD11c+ cells during TNF driven arthritis and K/BxN arthritis. In addition local bone destruction and the number of osteoclasts was significantly reduced. The number of CD115+ CD11b+ GR neg/low osteoclast precursors was significantly reduced in the

peripheral blood of CD11c-DTR transgenic mice that had received DT, suggesting a role of CD11c+ cells for osteoclast precursor generation.
Conclusion: These data show that CD11c + cells are involved in innate reactions leading to inflammatory arthritis and suggest that dendritic cells could be an important target for rheumatoid arthritis therapy.