levels were observed in the spleen when radio-resistant cells lack TLR4.

Conclusion These data suggest that TLR4 plays a role on both the bone marrow derived and local resident cells in aggravating experimental arthritis. TLR4 plays a role locally on the synovial fibroblasts by creating a more aggressive inflammatory environment in the joint cavity and thereby increasing joint destruction. Conversely, TLR4 activation on the bone marrow derived cells could increase T cell activation by antigen presenting cells and thereby promoting a more aggressive Th17 phenotype and increase joint swelling.

A97 IDENTIFYING THE TLR4 BEARING TARGET CELL IN EXPERIMENTAL ARTHRITIS

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Purpose The interleukin 1 (IL-1) receptor antagonist (IL-1Ra) knockout mice spontaneously develop T cell driven arthritis due to excessive IL-1 signalling. Joint destruction is accompanied by increased Th17 cells and elevated IL-17 levels compared to wild type (Balb/c) mice. When cross bred with toll-like receptor 4 (TLR4) knock out (TLR4^{-/-}) these animals showed reduced inflammation, joint destruction and diminished IL-17 levels. To reduce adverse effects of TLR4 inhibition a cell specific targeted therapy of arthritis is desired. Therefore, the authors set out to identify the TLR4 bearing cells in experimental arthritis responsible for increased IL-17 production and arthritis severity.

Method A reciprocal sex-mismatched bone marrow transplantation was performed with TLR4^{-/-} and TLR4^{+/+} mice in the IL-1Ra^{-/-} background and Balb/c bone marrow as control. Y-chromosome staining of bone marrow was performed to assess engraftment. Clinical manifestation of disease was assessed macroscopically over time. Spleen and lymph node cells were isolated and subjected to T helper subset analysis.

Results Engraftment of bone marrow was near 100% successful as determined by Y-chromosome staining of the bone marrow, which indicates a successful reconstitution. Lack of TLR4 on either the engrafted bone marrow cells or the radio-resistant cells in the joint did not affect disease incidence. However, animals that lacked TLR4 on the engrafted bone marrow derived cells, radio-resistant cells, or both showed reduced macroscopic arthritis scores. In mesenteric lymph nodes there were no differences observed in percentage of interferon γ and IL-17 producing cells. Neither was there a difference in Th1 cells in the spleen. However, decreased Th17