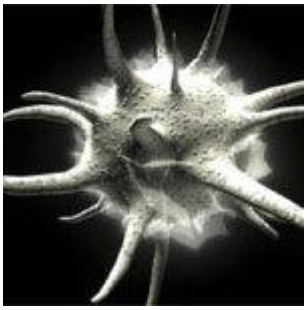
New Mechanism underlying Rheumatoid Arthritis Pathogenesis



Rheumatoid Arthritis (RA) is an autoimmune disorder that affects the joints and while the cause of RA is unclear, it is attributed to a combination of genetic and environmental factors. The present study, published in Annals of the Rheumatic Diseases, describes a new mechanism underlying RA. The experimental analyses were based on the C-type lectin receptors (CLRs), which are known to play a critical role in immune homeostasis. Loss or mutations in inhibitory CLRs have been linked to destructive autoimmunity.

The authors focused on the Myeloid inhibitory C-type lectin-like receptor (MICL) whose physiological function is unknown; and utilized MICL knockout mice (-/-) to determine the role of this C type lectin in RA inflammatory pathology. The knock out mice (-/-) were generated commercially and characterized using the collagen antibody-induced arthritis (CAIA) model. Mice samples were analyzed based on clinical scoring, histology, flow cytometry, irradiation bone-marrow chimera generation, administration of blocking antibodies and in vivo imaging. Human samples from patients with RA were also obtained for MICL characterization by immunohistochemistry and single nucleotide polymorphism analysis. Furthermore, anti-MICL antibodies were detected in patient serum by ELISA and dot-blot analysis.

The findings demonstrate MICL is required to control inflammation in murine models of collagen antibody-induced arthritis (CAIA). The MICL-deficient animals exhibited markedly exacerbated inflammation during CAIA, owing to the inappropriate activation of myeloid cells. In humans, this MICL was shown to be an auto antigen, the target of autoantibodies in a subset of patients with RA. This study demonstrates a new mechanism in RA inflammatory pathology indicating MICL plays an essential role in regulation of inflammation during arthritis and is an autoantigen in some patients with RA.

Redelinghuys, P. et al. 2015. MICL controls inflammation in rheumatoid arthritis. *Annals of Rheumatic Diseases.*