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Scientists discover new mechanism that leads to inflammation in rheumatoid arthritis

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New research findings published in the *Journal of Leukocyte Biology*, suggest that synovial CD4+ T cells that produce IL-21 contribute to joint inflammation by activating synovial fibroblasts in rheumatoid arthritis patients. Understanding the mechanisms of inflammation in rheumatoid arthritis is important for the design of new therapies for this disease.

"Patients with rheumatoid arthritis with active disease (inflamed joints) have difficulty for instance in using their hands and also with walking," said Maria Cristina Lebre, Ph.D., a researcher involved in the work from the Academic Medical Center at the University of Amsterdam, Department of Experimental Immunology in Amsterdam, The Netherlands. "New targeted therapies such as that proposed in this study (decrease in inflammation) will certainly improve the quality of life of patients by increasing their mobility."

Using a novel isolation method, scientists isolated T cells from synovial fluid from patients with rheumatoid arthritis that produced IL-21 and TNF and compared these with cells that did not produce this cytokine. When cells that produced IL-21 were put in culture with synovial fibroblasts (which are the main contributors to joint inflammation in rheumatoid arthritis), they induced the production of proinflammatory cytokines by these synovial fibroblasts, and cells that do not produce IL-21, did not demonstrate this same outcome. The results of this study suggest that a combined therapy targeting IL-21 and TNF might be beneficial for patients that do not respond to anti-TNF therapy or other current therapies. This research could also have an impact on other

diseases such as systemic lupus erythematosus, systemic sclerosis and Crohn's disease.

"Patients with rheumatoid arthritis often become refractory to treatment provoking the need to try different drugs targeting different pathways," said John Wherry, Ph.D., Deputy Editor of the *Journal of Leukocyte Biology*. "The identification of a new inflammatory target in rheumatoid arthritis holds promise for better treatment for these patients and perhaps those with other autoimmune or inflammatory diseases."

More information: Maria C. Lebre et al, Synovial IL-21/TNF-producing CD4T cells induce joint destruction in rheumatoid arthritis by inducing matrix metalloproteinase production by fibroblast-like synoviocytes, *Journal of Leukocyte Biology* (2017). DOI: 10.1189/jlb.5A0516-217RR

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