Autoimmune Th17 cells induced synovial stromal and innate lymphoid cell secretion of the cytokine GM-CSF to initiate and augment autoimmune arthritis

Keywords: rheumatoid arthritis, autoimmune disease, GM-CSF, Th17, inflammatory cytokine

- T cell production of GM-CSF is dispensable for the initiation of arthritis
- GM-CSF from stromal cells is crucial for the initiation of autoimmune arthritis
- GM-CSF-producing synovial-resident ILCs augment autoimmune arthritis
- ILC production of GM-CSF is stimulated by IL-2, IL-33, or TLR9 ligands

Abstract
Despite the importance of Th17 cells in autoimmune diseases, it remains unclear how they control other inflammatory cells in autoimmune tissue damage. Using a model of spontaneous autoimmune arthritis, Hirota and Sakaguchi’s group showed arthritogenic Th17 cells stimulated fibroblast-like synoviocytes via interleukin-17 (IL-17) to secrete the cytokine GM-CSF and also expanded synovial-resident innate lymphoid cells (ILCs) in inflamed joints. Activated synovial ILCs, which expressed CD25, IL33Ra, and TLR9, produced abundant GM-CSF upon stimulation by IL-2, IL-33, or CpG DNA. Loss of GM-CSF production by either ILCs or radioresistant stroma cells prevented Th17 cell-mediated arthritis. GM-CSF production by Th17 cells augmented chronic inflammation but was dispensable for the initiation of arthritis. The authors showed GM-CSF-producing ILCs were present in inflamed joints of rheumatoid arthritis patients. Thus, a cellular cascade of autoimmune Th17 cells, ILCs, and stroma cells, via IL-17 and GM-CSF, mediates chronic joint inflammation and can be a target for therapeutic intervention.

Graphical Abstract
Hirota et al. identified in an animal model of rheumatoid arthritis an inflammatory cellular cascade instigated by an arthritogenic T helper subset and enhanced by GM-CSF-producing synovial-resident innate lymphoid cells.
【Journal】Immunity (May 23, 2018 online)

【Article Title】
Autoimmune Th17 Cells Induced Synovial Stromal and Innate Lymphoid Cell Secretion of the Cytokine GM-CSF to Initiate and Augment Autoimmune Arthritis

【Authors】
Keiji Hirota, Motomu Hashimoto, Yoshinaga Ito, Mayumi Matsuura, Hiromu Ito, Masao Tanaka, Hitomi Watanabe, Gen Kondoh, Atsushi Tanaka, Keiko Yasuda, Manfred Kopf, Alexandre J Potocnik, Brigitta Stockinger, Noriko Sakaguchi, Shimon Sakaguchi