Conclusion: The GC genotype of IL-6-174 G/C was suggested by the analyses to be related to low prevalence of vasculitis, especially for large and medium vessels.

Methods: RA-FLSs were stimulated by TNF-α with or without pre-treatment of tofacitinib. The expression levels of VEGF, TNC and GLS were determined using reverse transcription-polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay (ELISA).

Results: In cultured RA-FLSs, VEGF, TNC and GLS were significantly induced by stimulation with TNF-α alone and these inductions were significantly suppressed by treatment of tofacitinib in a dose-dependent manner.

Conclusion: These findings indicate tofacitinib inhibits the VEGF, TNC and GLS production through blockade of a JAK/STAT pathway. Tofacitinib may extinguish inflammatory synovitis through preventing excessive angiogenic factors in RA-FLSs.

REFERENCES


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AB0069

THE DOWNSTREAM EFFECT OF ADALIMUMAB INVOLVES INHIBITION OF SYNOVIAL CXCL SUBFAMILY CHEMOKINE EXPRESSION

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Background: The many different disease modifying anti-rheumatic drugs used for the treatment of immune mediated inflammatory arthritis have very distinctive modes of action. However, the downstream effects of the different drugs are not completely understood. As more treatment options become available detailed knowledge about the different drugs will be important in the future when planning treatment strategies. Adalimumab is a fully humanized monoclonal antibody against tumor necrosis factor-alpha (TNFα). Earlier studies have found that TNFα inhibitors can decrease the production of interleukin 1 (IL-1), IL-6, IL-8 (aka CXC motif chemokine 8 (CXCL8)), monocyte chemotactic protein 1 (MCP-1) and granulocyte-macrophage colony-stimulating factor (GM-CSF).[1] However, these studies have been limited to the measurement of a subset of predefined downstream signaling molecules.

Objective: The aim of this study was to make an unbiased investigation of downstream effects of adalimumab on production of a wide range of cytokines, chemokines and growth factors by synovial fluid mononuclear cells (SFMCs).

Methods: SFMCs were obtained from a study population consisting of patients with active RA or peripheral SpA with at least one swollen joint (for obtaining synovial fluid) (n=14). SFMCs were cultured for 48 hours with and without addition of adalimumab 5 μg/ml measuring the secretion of 96 cytokines, chemokines and growth factors by an Olink proseek multiplex panel.

Results: In SFMCs cultured for 48 hours, adalimumab decreased the production of IL-8 (CXCL8) (P=0.0001), CXC motif chemokine 5 (CXCL5) (P=0.0003), CXCL9 (P=0.03) and CXCL10 (P=0.03), and monocyte chemotactic protein 2 (MCP-2) (P=0.04) and increased the production of hepatocyte growth factor (HGF) (P=0.008) and tumor necrosis factor-like weak inducer of apoptosis (TWEA) (P=0.03) after Bonferroni correction (all corrected P values). In this unbiased analysis, adalimumab did not change the production of several other non-significant chemokines.