Rheumatoid Arthritis & Cytokines

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease characterized by joint inflammation, the production of a wide assortment of cytokines, and ultimately joint destruction. The imbalance between pro-inflammatory and anti-inflammatory cytokines favors induction of RA. By promoting autoimmunity, maintaining chronic inflammatory synovitis, and promoting the destruction of adjacent joint tissue, cytokines have been implicated in each phase of the pathogenesis of this disease. For instance, IL-6 directly regulates the release of acute-phase proteins from hepatocytes and Kupffer cells. Meanwhile, TNFα is often targeted as a common treatment for RA.

Early studies associated RA primarily with T_{H}1 cytokines. Therefore, RA was considered a disorder driven by a population of T cells that produce inflammatory cytokines and chemokines such as IFNγ, LTα, and TNF. However, more recently, T_{H}17 cells have emerged as a key driver of inflammation and, therefore, rheumatoid arthritis. IL-17 is detectable in the rheumatoid synovium and joints of mice suffering from RA. Additionally, IL-17-deficient mice exhibit decreased disease severity, while those with higher IL-17 levels display exacerbated disease. Furthermore, patients with RA have been shown to respond to treatment with anti-IL-17 monoclonal antibodies.

An important feature of rheumatoid arthritis synovitis is the relatively reduced expression of several inhibitory cytokines that creates an imbalance between pro-inflammatory and the anti-inflammatory cytokines in the joints. IL-1RA, IL-10, and IL-11 are detected in this tissue, but not at sufficient concentrations to counterbalance the activity of pro-inflammatory cytokines. Additionally, IL-2 and IL-4 are absent, thereby impairing T_{H}2 cell development in favor of T_{H}1 and T_{H}17 cell differentiation. As this autoimmune disease demonstrates, cytokine expression must be carefully regulated in order to maintain an appropriately functioning immune response.