"Novel Cytokines in Infection And Inflammatory Diseases”

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Abstract

Cytokines are hormones of the immune system and play a pivotal role in immune response. Cytokine targeting is arguably the most important recent contribution of immunology to clinical practice. I will discuss the role of IL-33 and IL-35 in inflammation.

IL-33, the latest member of the IL-1 family, is the ligand of ST2 which is expressed on Th2 cells and mast cells. IL-33 can skew a predominantly Th1 cell population to a mainly Th2 cells phenotype in vivo. IL-33 mRNA is expressed early during infection of the intestinal-dwelling nematode *Trichuris muris* in mice. IL-33 treatment enhances resistance to the infection. Thus IL-33 may be evolutionally preserved for the host defense against parasitic infection. Furthermore, IL-33 can reduce an ongoing atherosclerosis in ApE−/− mice. It can also attenuate experimental sepsis. Patients with severe sepsis have reduced levels of IL-33. However, IL-33 is a double-edged sword. It can also enhance allergic reaction and inflammatory disease such as arthritis and asthma.

IL-35 is the latest member of the IL-12 family. It is formed by pairing Epstein-Barr virus-induced gene 3 (EBI3) and the p35 subunit of IL-12. IL-35 induces proliferation of murine CD4+CD25+ T cells in vitro. The IL-35-expanded CD4+CD25+ Foxp3+ T cells retain their suppressive functions against CD4+CD25+ effector cells. In vivo, IL-35 attenuates established CIA in mice with concomitant suppression of IL-17 production but enhanced IFNγ synthesis. Thus IL-35 is a novel anti-inflammatory cytokine suppressing the immune response through the expansion of regulatory T cells and suppression of Th17 cell development.

Research interests

The immune system is normally tightly regulated to achieve a state of homeostasis. There are a number of ways to achieve this balance of which cytokines are major mediators. Cytokines form a network by which the various effector cells of the immune system interact with each other to maintain a balance between defence against infections and sufficient tolerance to avoid autoimmune diseases. We have focused our research on the role of TLR2, IL-33 and nitric oxide on the regulation of the immune response, with particular interest in the modulation of regulatory T cells by TLR2 and NO. IL-33 is a novel cytokine and an agonist of ST2, a gene product preferentially expressed on a subset of Th2 cells.

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