第二十三介白質角色與抗二十三介白質治療

The role of interleukin-23 and anti-interleukin-23 therapy.

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Abstract

Interleukin-23 (IL-23) is a heterodimer proinflammatory cytokine composed of two proteins subunits, the p40 subunit that is shared with IL-12, and a unique p19 subunit [1, 2]. IL-23 is mainly secreted by activated macrophages, dendritic cells, and non-immune cells, including keratinocytes and synoviocytes [3, 4]. The signaling of IL-23 receptor is mediated by Janus kinase (JAK) family members. Upon ligation to IL-23, the JAK members activates and phosphorylates both signal transducers and activators of transcription (STATs) followed by homodimerization of the STATs molecules and then translocation into the nucleus for transcription. The activation can enhance the expansion of T helper type 17 (Th17) cells, and is responsible for many of the inflammatory autoimmune responses [5]. A variety of cells bear IL-23 receptors. IL-23 can also activate NK cells, enhance T-cell proliferation, and regulate antibody production [5, 6].

IL-23 plays a role in the center of inflammation. A wide spectrum of pathogen-associated molecular patterns and cytokines can trigger IL-23-mediated inflammatory response [1]. Dysregulation of IL-23-mediated inflammatory response can cause chronic inflammation and tissue damage since both IL-17 and IL-22 axes can promote positive feedback loops, leading to inflammation permanence. Dysregulated and Increased amounts of IL-23 are associated with a number of autoimmune diseases, including psoriasis, rheumatoid arthritis and inflammatory bowel diseases [1, 5, 6].

The increased activity of IL-23 in autoimmune diseases allowed its targeting as a therapy. The inhibition of IL-23 might be a novel and promising therapeutic strategy [1, 5]. This was found to be effective and associated with disease remission proven by clinical trials, such as ustekinumab, which prevents IL-12 and IL-23 from interacting with the surface receptor. Novel therapeutic strategies will now focus on the targeting of IL-12 and IL-23 separately [7]. IL-23-based therapy can include either IL-23 antagonists which are mainly antibodies (risankizumab, guselkumab, tildrakizumab, etc.), or IL-23 receptor downstream signaling suppressors such as JAK inhibitors (tofacitinib, baricitinib, peficitinib, etc.) [1, 6, 8]. Although IL-23 is responsible for many autoimmune diseases, there is still work to be done before achieving even greater frequency of complete and durable clinical remission in its immunology trials.

References

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