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NEW CYTOKINES INVOLVED IN SMALL BOWEL INFLAMMATION

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ANNOTATSIYA

Inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), is a group of chronic diseases characterized by gastrointestinal inflammation, usually with a recurrent and transient clinical course. Mucosal macrophages play an important role in the mucosal immune system, and increased numbers of newly recruited monocytes and activated macrophages have been reported in the inflamed intestine of patients with IBD.

Introduction: Inflammatory bowel disease (IBD) includes two forms: ulcerative colitis (UC) and Crohn's disease (CD). The pathogenesis of UC and CD is currently not fully understood, although chronic recurrent inflammation is thought to result from a dysregulated aberrant immune response to intestinal flora in the context of genetic predisposition. In ECD, this loss of immune tolerance to intestinal flora is mediated by various molecules. Cytokines are key signals in the gut immune system and are known to be involved in the disruption of the so-called normal state of controlled inflammation (physiological gut inflammation) [1]. Cytokines are small peptide proteins produced mainly by immune cells that facilitate cell-to-cell communication, stimulate the proliferation of antigen-specific effector cells and mediate local and systemic inflammation in autocrine, paracrine and endocrine pathways [2]. The innate immune response plays a crucial role in ECD. Activated dendritic cells (DCs) and macrophages secrete several cytokines that actively regulate the inflammatory response in UC and CD Once these cytokines are secreted by these antigen-presenting cells (APC), they trigger and differentiate a multitude of T cells, activating an adaptive immune response. VZC also has a dysregulation of T cells, with impaired clearance of over-reactive and autoreactive cells, in addition to an imbalance of Treg/ Th1, Th2 and the recently described Th17 cell populations in the activated state. Lack of appropriate regulation by T cells or overproduction of effector T cells is involved in the development and exacerbation of IBD [3].

Overall, APC, Th1, Th2, T regulatory cells and the recently characterized Th17 and their cytokine products play a complex role in IBD [4]. These cellular interactions are modulated by both traditionally studied cytokines (such as TNF-α, INF-γ, IL-1, IL-6, IL-4, IL-5, IL10, TGF-β) and others, recently characterised (such as IL -13, IL-12, IL-18, IL-23), which are thought to be pro- or anti-inflammatory. Although many common responses in ECD are mediated by cytokines, such as regulation of the production of inflammatory mediators, active oxygen metabolites, nitric oxide, leukotrienes, platelet-activating factor and prostaglandins, activation of nuclear factor κB (NF-κB) and inhibition of apoptosis, how cytokines determine the nature of the immune response in ECD can vary widely among forms of ECD [6]. CD is associated with a Th1-T cell-mediated response characterised by increased production of IFN-γ and TNF-α. IL-12 and IL-23 regulate Th1 differentiation, which in combination with IL-15, IL-18 and IL-21 causes stabilisation of polarised Th1. On the other hand, in UC, the local immune response is less polarised, but it is characterised by the production of CD1-reactive natural killer T cells by IL-13 and the production of Th2 cytokines. Other cytokines, such as IL-21 and IL-22, which are involved in the pathophysiology of inflammatory and autoimmune diseases such as asthma, arthritis and lupus, also play important roles in IBD. IL-21 is a cytokine originating from T cells, a member of the general family of gamma-chain-dependent cytokines, which generally acts on the intestinal epithelium to help maintain ongoing Th1 inflammation by inducing IFN-γ production [2]. IL-21 has also been shown to enhance the growth of NK cells [5]. IL-21 is expressed by immune T- and B-cells and by non-immune cells such as fibroblasts, where it activates metalloproteinase 1 production, and by signalling through its receptor IL-21R, it activates STAT-3 in T-cells IL-21, like IL-6 and IL-23, is also involved in Th17 cell differentiation and is overexpressed in both CD and UC, with higher levels found in CD . IL-22 was originally described as an inducible IL-9 gene and named as an inducible T-cell-derived factor related to IL-10 (IL-TIF) . This cytokine shows 22% amino acid identity with IL-10 and belongs to the cytokine family with limited homology to IL-10. IL-22 binds on the cell surface to a receptor complex consisting of two chains belonging to cytokine receptor class II (CRF2) family: IL-22R1 and IL-10R2. In intestinal cells, especially in innate immune cells, binding of IL-22 to its corresponding R1 chain causes a conformational change that allows IL-10R2 to interact with newly formed ligand-receptor complexes. This in turn activates a signal transduction cascade that leads to the rapid activation of several transcription factors, including STAT1/ 3 proteins. The main sources of IL-22 are natural killer cells and activated T and B cells. Th17 has proved a very important role in this issue . IL-22 has pro-inflammatory functions in IEC and is activated in CD in both tissue and serum. Unexpectedly in a mouse model of UC Sugimoto et al. demonstrated a novel protective role for IL-22, in which IL-22 attenuates intestinal inflammation by inducing membrane-bound mucin formation by bokalovid cells . Other recent work has shown that IL23R genotypes affect serum IL-22 concentrations, linking genetic susceptibility to CD to Th17 cell function for the first time.

Conclusions: Cytokines play an important role in the pathogenesis of IBD, and their manipulation successfully reduces disease severity and supports remission. Following the discovery of new cytokines and the role they may play in intestinal mucosal immunity, as well as new concepts and paradigm shifts in the pathogenesis of IBD, the role of several cytokines has been clarified and tested in both preclinical animal models and in clinical trials. patients with IBD. In addition to this, proof of concept for novel cytokine targets is rapidly evolving, with the possibility of future cytokine-based therapies that may offer greater specificity and reduced toxicity for the treatment of IBD. In addition, further applications of cytokine-based therapies in human clinical trials and preclinical animal studies are ongoing.

Foydalanilgan adabiyotlar:

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