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Letter to the Editor

IL-37 is an inhibitory cytokine that could be useful for treating infections

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INTRODUCTION

Interleukin (IL)-37 is an anti-inflammatory cytokine that plays a crucial role in modulating the immune response. IL-37 acts by limiting excessive inflammation and protecting tissues from damage. IL-37 is a member of the IL-1 family and is a cytokine that inhibits both innate and adaptive immunity. When it binds to the IL-18 receptor (IL-1R5) (IL-18 is a proinflammatory protein), this cytokine has an anti-inflammatory effect.

DISCUSSION

IL-37 binds to IL-1R5, forming a complex with the IL-1R8 receptor that has anti-inflammatory properties (1 Sanchez). This complex dampens pro-inflammatory signaling pathways. The presence of IL-1R8 is essential, as the lack of this receptor does not allow IL-37 to carry out its anti-inflammatory effect. Among the biological effects of IL-37, there is the anti-tumor effect that it exerts on natural killer (NK) cells, on which IL-37 causes an increase in anti-tumor stimulation, a characteristic possessed by NK. These effects of IL-37 on NK cells also occur in the absence of the IL-1R8 receptor.

IL-37 is produced as an inactive precursor and requires processing by caspase-1 to become active. The active form of IL-37 can be secreted extracellularly or can function intracellularly. The effect of IL-37 on innate immunity occurs through the inhibition of the mammalian target of rapamycin (mTOR) signaling pathway, increased oxidative phosphorylation of the kinase, and reduction of succinate. IL-37 translocates to the nucleus, where it binds to SMAD3, a transcription factor involved in transforming growth factor-β (TGF-β) signaling.

IL-37 is produced by macrophage and dendritic cells, protagonists of innate immunity. IL-37 also plays a crucial role in acquired immune responses, acting on dendritic cells by causing them to produce high levels of the inhibitory cytokine IL-10 which participates in immune tolerance. IL-37 also has an inhibitory effect on antigen presentation by major histocompatibility complex Class II (MHCII). Mice with rheumatoid arthritis that were treated with this cytokine showed a reduction in joint inflammation (2 Dinarello). IL-37 has also been shown to be useful in the experimental treatment of mice with streptococcal infection, an effect that did not occur in mice in which the IL-1R8 receptor was suppressed (3 N-P). In addition, IL-37 can control inflammatory complications in viral diseases including influenza and COVID-19 (4 Su), however, excessive IL-37 can potentially interfere with antiviral immunity.

The anti-inflammatory action of IL-37 occurs mostly through its inhibition of IL-1, but also of tumor necrosis factor (TNF), IL-6, IL-17, and the chemokine CCL2. Subjects with deficient levels of IL-37 may be more likely to experience

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inflammatory diseases and also have more pronounced inflammation in infectious diseases (4 Su). IL-37 mitigates the "cytokine storm" by reducing excessive inflammation. For example, in sepsis or viral infections, IL-37 limits tissue damage caused by overactive immune responses. T lymphocytes, which play an important role in infections, may be more activated in IL-37 deficiency, which contributes to the pathological damage.

CONCLUSIONS

Levels of IL-37 are increased in many inflammatory diseases, including psoriasis, arthritis, systemic lupus erythematosus, ankylosing spondylitis, allergic rhinitis, cancer, and periodontitis. The increased levels of IL-37 in inflammatory diseases are due to the organism's reaction in response to tissue inflammation, whereas decreased IL-37 seems to contribute to the severity of inflammation. Modulating IL-37 activity selectively during infections may offer novel therapeutic strategies for conditions characterized by immune dysregulation.

Conflict of interest

The author declares that they have no conflict of interest.

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