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The Pathophysiology and Role of IL-7 in the Immune Response and Autoimmune Diseases: A Review Article

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ABSTRACT: IL-7 is one of the very important cytokines in the regulation and maintenance of immune responses. IL-7 has been described as a very pivotal lymphocyte development, homeostasis, and activation mediator. Recent studies focused on the pathways influenced by IL-7 and their role in innate and adaptive immunities. Interleukin-7 (IL-7) is a critical cytokine in the development and homeostasis of T cells, as well as the signaling of other immune cells, such as natural killer (NK) cells. IL-7 signaling is also important for the majority of T cell functions and disease associations, which include protection against infectious diseases, autoimmunity, and tumor malignancies. This paper reviews the current findings on IL-7 and its role in the immune response, with particular emphasis on the mechanisms of signaling pathways it induces and its effects on lymphocyte functions, therefore opening a window for a future therapeutic application. It also presents recent research findings on the role of IL-7 in the diseased state dynamics of many illnesses, which consequently underscores possible therapeutic applications while simultaneously pinpointing the shortcomings in the existing knowledge regarding the biology of IL-7.

INTRODUCTION

The IL-7 signaling pathway is predominantly through Jak-STAT. The receptor for IL-7 (IL-7R) when bound initiates Jak3 which subsequently leads to the phosphorylation of STAT5. The activation of STAT5 therefore represents a vital mechanism through which transcriptional programs driving T cell survival and expansion are established (Villarino et al., 2017). A recent study indicates that m6A mRNA methylation involves and permits further modulation of IL-7 signaling through the IL-7/STAT5 pathway, hence revealing the intricate post-transcriptional regulation during immune homeostasis (Li et al., 2017).

IL-7 also engages other immune pathways in innate immunity. IL-7 can upregulate functions of innate lymphoid cells, which is a cell type critical for tissue homeostasis and robust responses to infection (Monticelli et al., 2011). The relationship between IL-7 and innate immunity demonstrates that the role of IL-7 is not limited to T cell biology but rather encompasses a broad involvement in immune responses.

IL-7 is critical regarding T cell homeostasis and survival. It has been demonstrated specifically that it prevents apoptosis of T cells during sepsis, thereby promoting both the viability and functionality of T cells (Unsinger et al., 2010). Such an effect is important because severe infections may cause immune suppression with a characteristic depletion of T cells. The anti-apoptotic effects of IL-7 are achieved through different signaling pathways, far leading to increased expression of adhesion molecules and decreased pro-apoptotic factors (Malhotra et al., 2012). Also, IL-7 does not benefit only T cells but also sustains proliferation and survival of NK cells; those are key elements in anti-tumor as well as anti-viral responses (Abel et al., 2018).

Though the functions of IL-7 in adaptive and innate immunity have been described, several angles of ignorance still persist. One of them is the exact interaction patterns between IL-7 and other cytokines and immune pathways. Another one is the previously established signaling biochemistry of IL-7, but the influence of various post-translational modifications on IL-7 functionality remains to be determined. The potential of IL-7 as a therapeutic agent in many diseases, including cancer and autoimmunity, has not been sufficiently studied. However, knowledge on how to control IL-7 signaling may ultimately engender new treatments to boost immune responses in immunocompromised states or dampen such responses in autoimmune conditions.

Despite the many studies conducted on IL-7, there are still gaps in our knowledge. One example is the poorly understood mechanisms by which IL-7 participates in the T cell dysregulation often seen in autoimmune diseases. Another point is the increasing role of IL-7 in sepsis and viral infections which becomes clearer day by day; however, its relations with other inflammatory cytokines in different pathological settings are poorly understood and need more studies. Research efforts should be directed toward the recently discovered biphasic activity of IL-7 in driving protective as well as pathogenic immune responses. Such studies may open

new avenues for the therapeutic use of IL-7 together with other cytokines in autoimmune diseases, infections, and cancers. Long-term effects of IL-7 modulation on immune memory and duration of response also need to be defined to build immunotherapy based on IL-7.

ROLE OF IL-7 IN IMMUNE RESPONSE

The function of IL-7 in T cell homeostasis has already been greatly established. It is necessary for the survival of naive and memory T cells, and thus the levels of this cytokine directly influence T cell populations in peripheral tissues. Lack of IL-7 leads to a decrease in the number of T cells and impaired immune responses (Kumar et al., 2011). In addition, the expression of IL-7 and chemokines such as CCL19 in CAR-T cells has been associated with improved immune cell infiltration and enhanced CAR-T cell survival within tumors; therefore, it can be presumed that IL-7 may have a therapeutic application in cancer immunotherapy (Adachi et al., 2018).

The role of IL-7 also involves inflammation, where it possibly takes part in the cascade of double-edged actions. On one side, IL-7 is needed to properly respond to infections; on the other side, high levels of signaling IL-7 have been linked with chronic cases of inflammation (Zhao et al., 2021). The proper balance between sufficient levels of IL-7 to activate immunity and overactivation and its consequences for inflammation is therefore a very pertinent field of research.

Psoriasis and other autoimmune diseases have a very complex interplay of immune responses and cytokines in their pathophysiology. Though IL-7 does not participate directly in inflammatory processes in psoriasis, its involvement in T cell homeostasis makes it possible that it influences disease severity and response to treatments directed against other cytokines (Armstrong & Read, 2020). IL-7 is suggested to further immune dysregulation in autoimmune diseases; therefore, such a cytokine might exert dual roles in support of both protective and pathogenic T cell responses. In rheumatoid arthritis (RA), IL-7 might affect macrophage polarization and T cell responses, perpetuating inflammation (Branchford & Carpenter, 2018). Novel therapeutic approaches may arise from understanding the interactions of IL-7 with other cytokines in these maladies.

The importance of IL-7 extends to viral infections as well, especially HIV-1, in which the signaling is hampered, eventually culminating in the depletion of T cells (Schett et al., 2017). One potential area of therapeutic application for IL-7 is where it might restore immune functions in HIV-1 infected patients. Studies have shown that IL-7 may facilitate immune reconstitution T Cell survival and function, T cells being the hallmark for recovery from dreaded infections (Unsinger et al., 2010).

Also, the bond between IL-7 and IL-15 in boosting memory T cell life during viral infections has been looked at, pointing out different but helpful ways for T cell stay and success. This interaction needs more study, particularly for vaccine creation and immunotherapy. The mechanism through which IL-7 operates involves the binding of this cytokine to its specific receptor, thereby activating downstream pathways, among which the more prominent is the STAT5 pathway (Li et al., 2017). This pathway mediates the survival signals that always give hope whenever IL-7 is applied. The role of IL-7 in T cell differentiation coupled with its potential interaction with other cytokines such as TSLP offers another immune response approach that seems very complex (Heerspink et al., 2019). TSLP, a similar signal through the IL-7 receptor, can be involved in further modulation of T cell responses during allergic and inflammatory conditions thereby suggesting an involvement as a potential therapeutic target in diseases characterized by Th2 responses. In keloid and hypertrophic scars, though IL-7 is not directly referred to, its role in immune modulation and tissue repair might help in comprehending the inflammatory processes involved in abnormal scar formation. Studying the effect of IL-7 on fibroblast activities and collagen deposition can create opportunities for directed treatments to modify outcomes in patients with problematic scars (Berman et al., 2017).

IL-7 was recently identified as a co-stimulatory factor for ILC2s, which participate in type 2 inflammation and tissue repair. Further understanding of the regulatory mechanisms of IL-7 on ILC2 activity may open new therapeutic windows for diseases featuring dysregulated type 2 inflammation (Kondo et al., 2021).

IL-7 is critical in memory T cell population dominance during viral infections. The balance between IL-7 and IL-15 in the regulation of T cell homeostasis applies to strategies directed toward optimization of antiviral immunity as well as improving vaccine applications (Romee et al., 2018).

IL-7 IN AUTOIMMUNE AND CARCINOGENIC DISEASES

Psoriasis is a chronic inflammatory skin disease with impaired immune regulation. Psoriasis pathogenesis involves T cell differentiation and proliferation, -IL-7 indirectly associated. The interaction of IL-7 with other cytokines, like IL-17 and TNF-α, indicates that the inhibition of IL-7 signaling might open new avenues in the therapeutic management of psoriasis and its comorbidities (Armstrong & Read, 2020).

In the context of RA, IL-7 has been shown to promote T cell survival and proliferation, which contributes to synovial inflammation and joint destruction. Targeted modulation of IL-7 signaling may represent a promising strategy for pharmacological intervention in symptom alleviation and disease modification in patients with RA (Köhler et al., 2017).

Research suggests that IL-7 is crucial for the stimulation of MAIT cells and their mucosal production of IL-17, which is a cytokine linked to the inflammatory mechanisms of AS. This underlines the possibility of IL-7 as a pharmacological endpoint to alter inflammation and result for patients with AS betterment (Schett et al., 2017).

IL-7 is important for the development and activity of natural killer cells. The natural killer cells are very important in anti-tumor and anti-viral activities. Boosting IL-7 activity in natural killer cells may open new ways of immunotherapy in cancer by boosting treatment efficiencies against tumors and viral infections (Abel et al., 2018). Another example is the clinical relevance of IL-15, a cytokine similar to IL-7, which improves immune responses after transplantation thus underlining the role of such cytokines in cancer therapy (Propper & Balkwill, 2022).

CONCLUSION

In conclusion, IL-7 is a critical cytokine in the orchestration of immune responses-a prime pillar for basic immunology and clinical applications. Though much has been learned about its biochemical pathways and roles in T cell homeostasis and inflammation, the potential aspect concerning its therapeutic contexts remains obscure. However, as the field progresses, IL-7 might become that prospective key target for delivery through novel immunotherapeutic strategies. IL-7 is a pivotal cytokine with fundamental role in T cell homeostasis, survival, and immune modulation. The significance of its mechanisms of action and involvement in various diseases makes such studies indispensable. A comprehensive understanding of the multifaceted nature of IL-7 is likely to not only enrich the immune regulation knowledge base but also lead to new therapeutic strategies in immunological disorders. IL-7 has come forward as one of the major cytokines with unambiguous implications in the pathophysiology of disease processes, including autoimmunity, malignancy, and chronic inflammatory conditions. Knowledge of its mechanisms of action and interplay with other cytokines will facilitate the construction of new therapeutic strategies. As the research trends change, filling in the already established gaps will be integral in maximizing the use of IL-7 in clinical applications.

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