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The Role of IL-11 in Regenerative Medicine and Tissue Engineering

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Abstract

Interleukin-11 (IL-11) is a crucial cytokine in regenerative medicine and tissue engineering due to its role in tissue repair, cellular regeneration, and immune responses. It involves various biological processes, including hematopoiesis, inflammation, and remodeling. IL-11 is essential for maintaining progenitor cell populations during regeneration, enhancing wound healing, and modulating fibrotic responses during tissue repair. It also influences the immune microenvironment, promoting a reparative M2 phenotype conducive to tissue healing. IL-11's role in bone metabolism and repair is gaining attention, as it regulates the activity of osteoblasts and osteoclasts, influencing bone homeostasis and regeneration. IL-11's therapeutic applications extend beyond direct tissue repair and hold promise for improving the efficacy of biomaterials used in tissue engineering. However, the potential for IL-11 to induce adverse effects, such as excessive fibrosis, necessitates careful consideration in therapeutic applications. The interplay between IL-11 and the extracellular matrix (ECM) is another critical aspect of its role in regenerative medicine.

Keywords: Regenerative Medicine; Tissue Engineering; Interleukin-11 (IL-11)

Interleukin-11: A Key Cytokine in Regenerative Medicine and Tissue Engineering

Interleukin-11 (IL-11) is emerging as a pivotal cytokine in regenerative medicine and tissue engineering, primarily due to its multifaceted roles in tissue repair and cellular regeneration. As a member of the IL-6 family of cytokines, IL-11 has been implicated in various biological processes, including hematopoiesis, inflammation, and tissue remodeling, making it a critical factor in regenerative therapies [1-3]. One of the most significant aspects of IL-11's role in regenerative medicine is its ability to modulate the behavior of stem and progenitor cells. For instance, it demonstrated that IL-11 is essential for maintaining progenitor cell populations during the regeneration of Xenopus tadpole tails, indicating its potential to influence stem cell dynamics in regenerative contexts [1]. This finding is further supported by evidence that IL-11 can sustain the expression of undifferentiated markers in human embryonic stem cells, suggesting its utility in stem cell therapies and tissue engineering applications [1,2]. Moreover, IL-11 has been shown to enhance wound healing processes, particularly in ocular tissues. 's research highlights how IL-11 suppresses inflammation and accelerates the transformation of quiescent keratocytes into active fibroblasts, which are crucial for corneal repair [4].

Moreover, IL-11 is essential in modulating fibrotic responses during tissue repair. Studies have demonstrated

that IL-11 signaling in endothelial cells antagonizes profibrotic pathways, specifically those mediated by transforming growth factor-beta (TGF-β), thereby limiting fibrotic scarring and promoting the repopulation of cardiomyocytes following injury [5]. This finding underscores the potential of IL-11 as a therapeutic target for enhancing tissue regeneration while minimizing adverse fibrotic outcomes. In addition, the pro-regenerative effect of IL-11 also underscores its potential application in ocular regenerative therapies, where rapid and effective healing is paramount. In the context of fibrosis and tissue remodeling, IL-11's role becomes more complex. It has been reported that IL-11 can drive a profibrotic phenotype in various cell types, including fibroblasts in thyroid-associated ophthalmopathy [6].

This duality presents a challenge in therapeutic contexts, as while IL-11 can promote tissue repair, it may also contribute to pathological fibrosis if not adequately regulated [7]. Understanding the balance between these opposing roles is crucial for harnessing IL-11's regenerative potential without inducing adverse fibrotic responses. The signaling pathways activated by IL-11 are also of significant interest in regenerative medicine. IL-11 primarily signals through the STAT3 pathway, which regulates various cellular processes, including survival, proliferation, and differentiation [8]. The activation of STAT3 by IL-11 has been linked to neuroprotective effects and the modulation of immune responses, further emphasizing its potential in treating neurodegenerative diseases and enhancing tissue repair in the central nervous system [8]. In addition to its direct effects on cells, IL-11 also influences the immune microenvironment, critical for effective tissue regeneration. For example, IL-11 can modulate macrophage polarization, promoting a shift towards a reparative M2 phenotype that is conducive to tissue healing [9]. This macrophage polarization is essential in orchestrating the inflammatory response and facilitating the transition from inflammation to tissue repair, highlighting IL-11's role as a mediator of immune-stroma interactions [9].

Furthermore, IL-11's involvement in bone metabolism and repair is gaining attention. Recent studies have shown that IL-11 regulates the activity of osteoblasts and osteoclasts, thereby influencing bone homeostasis and regeneration [10]. This is particularly relevant in bone injuries and diseases, where enhancing IL-11 signaling could promote more effective healing and recovery. The therapeutic applications of IL-11 extend beyond direct tissue repair; it also holds promise for improving the efficacy of biomaterials used in tissue engineering. For instance, combining IL-11 with acellular biomaterials has improved wound healing outcomes through paracrine signaling mechanisms [11]. This synergistic approach could lead to more effective regenerative strategies that leverage cytokines signaling and biomaterial scaffolding. However, the potential for IL-11 to induce adverse effects, such as excessive fibrosis, necessitates careful consideration in therapeutic applications. Studies have indicated that high levels of IL-11 can disrupt the function of alveolar epithelial progenitor cells, leading to impaired lung repair [7]. This underscores the importance of dose regulation and timing in IL-11-based therapies to maximize benefits while minimizing risks.

The interplay between IL-11 and the extracellular matrix (ECM) is another critical aspect of its role in regenerative medicine. The ECM provides structural and biochemical support to surrounding cells, and its composition can significantly influence cellular behavior during regeneration. Note that the secretome of adipose tissue-derived stem cells, which includes various interleukins, plays a vital role in modulating the ECM and promoting regeneration [12]. IL-11's involvement in this process suggests that it could be a key player in enhancing the regenerative potential of stem cell therapies by influencing ECM dynamics.

Conclusion

IL-11 plays a multifaceted role in regenerative medicine and tissue engineering, influencing stem cell dynamics, wound healing, immune responses, and tissue remodeling. Its ability to modulate regenerative and fibrotic processes presents opportunities and challenges for therapeutic applications. Future research should focus on elucidating the precise mechanisms of IL-11 action, optimizing its use in clinical settings, and developing strategies to mitigate potential adverse effects associated with its pro-fibrotic properties.

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