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Editorial

The Importance of Mesenchymal Stromal/Stem Cell Therapy for Cancer

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Abstract

Mesenchymal stromal/stem cell (MSC) therapy has emerged as a transformative strategy in cancer treatment, leveraging the unique regenerative and immunomodulatory properties of MSCs to address the limitations of traditional approaches. This comprehensive review delves into the multifaceted applications and intricate mechanisms of action underlying MSC therapy for cancer. MSCs exhibit remarkable tumor-targeting capabilities, harnessing their innate homing abilities for selective migration to tumor sites. This property is harnessed for targeted drug delivery, optimizing therapeutic efficacy while minimizing collateral damage to healthy tissues. Moreover, the immunomodulatory prowess of MSCs plays a pivotal role in shaping the tumor microenvironment. Through the suppression of pro-inflammatory signals and the promotion of antitumor immune responses, MSCs create a milieu that inhibits tumor growth. Engineered MSCs further serve as carriers for anticancer drugs, facilitating direct delivery to tumor sites and mitigating systemic toxicity. Additionally, the radioprotective effects of MSCs provide a unique opportunity to enhance the therapeutic window during radiotherapy, safeguarding healthy tissues. However, challenges such as achieving consistent tumor tropism, addressing safety concerns, and standardizing protocols underscore the need for ongoing research. Rigorous clinical trials are imperative to establish the safety profile and efficacy of MSC therapy across diverse cancer types. As we navigate these challenges, the promise of personalized and effective cancer treatments through MSC therapy continues to unfold, offering new hope for improved outcomes in the relentless battle against cancer.

Keywords: mesenchymal stromal/stem cells (MSCs), cancer therapy, tumor targeting, immunomodulation, drug delivery

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1. Introduction

Cancer remains a pervasive global health challenge, necessitating innovative therapeutic strategies to enhance treatment efficacy and mitigate the limitations of conventional approaches [1]. Among the emerging paradigms, mesenchymal stromal/stem cell (MSC) therapy has emerged as a promising frontier in cancer treatment, capitalizing on the distinctive regenerative and immunomodulatory properties inherent in MSCs [2]. This comprehensive review aims to unravel the multifaceted applications and intricate mechanisms of MSC therapy in the context of cancer.

MSCs known for their ability to differentiate into various cell types and modulate immune responses, have gained prominence for their potential in reshaping the landscape of cancer therapy [3]. Notably, MSCs exhibit an inherent capacity for targeted tumor homing, enabling precise delivery of therapeutic payloads to malignant sites [4]. This ability holds significant promise for optimizing drug delivery, thereby enhancing the therapeutic index while minimizing adverse effects on healthy tissues [5].

In addition to their tumor-targeting prowess, MSCs exert profound immunomodulatory effects, orchestrating a complex interplay within the tumor microenvironment [6]. By modulating immune cell activity, MSCs create an environment conducive to suppressing tumor growth and fostering anticancer immune responses [7]. Furthermore, the engineering of MSCs as drug carriers presents an innovative avenue for localized drug delivery, reducing systemic toxicity and improving treatment outcomes [8].

As we navigate through the intricacies of MSC therapy for cancer, this review will delve into the diverse applications, mechanisms of action, and current challenges that necessitate rigorous exploration. The exploration of MSC therapy's potential holds the promise of not only enhancing the precision of cancer treatment but also opening new avenues for personalized and effective therapeutic interventions in the dynamic landscape of oncology.

2. Applications of MSC Therapy in Cancer

2.1. Tumor targeting

MSCs possess a unique ability to home in on tumor sites selectively [9]. This homing mechanism allows for targeted drug delivery, enhancing the therapeutic effects while minimizing damage to healthy tissues [10] (Figure **1**).

2.2. Immune modulation

The immunomodulatory properties of MSCs play a crucial role in shaping the tumor microenvironment [12]. By suppressing pro-inflammatory signals and promoting antitumor immune responses, MSCs create an environment unfavorable for tumor growth [13] (Figure **2**).

2.3. Drug delivery

Engineered MSCs can serve as carriers for anticancer drugs, providing a means to deliver therapeutic agents directly to the tumor site [4]. This targeted drug delivery approach improves drug bioavailability and reduces systemic toxicity [15].

2.4. Radioprotection

MSCs have demonstrated radioprotective effects, shielding healthy tissues during radiotherapy [16]. This capability enhances the therapeutic window for radiation treatments, allowing for more effective cancer management [17].

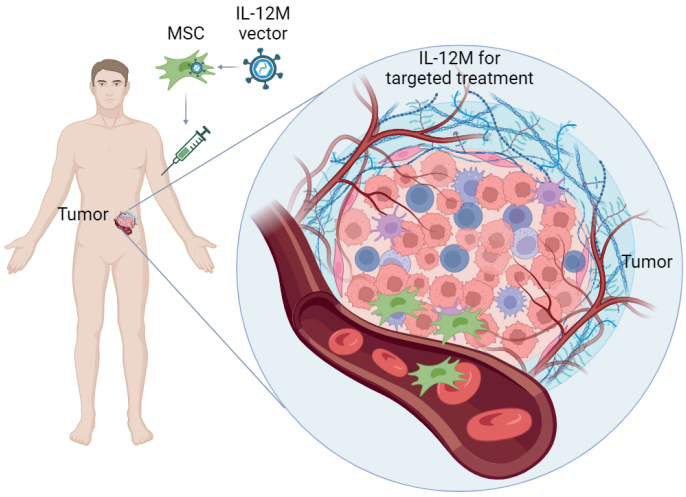

Figure 1: Diagrammatic representation of engineered mesenchymal stromal/stem cells (MSCs) therapy that expresses IL-12M for the focused treatment of cancer through tumor tropism. MSCs can serve as a carrier for cytokine transgene expression systems targeted to tumor sites [11].

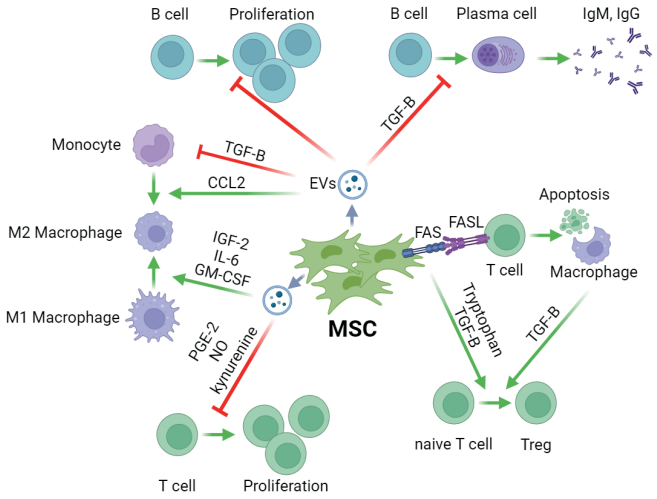

Figure 2: The primary pathways through which mesenchymal stromal/stem cells (MSCs) exert their immunoregulatory effects involve the production of metabolites, cytokines, growth factors, chemokines, extracellular vesicles, apoptotic vesicles, and T-cell death-mediated immunoregulation. MSCs possess the capability to hinder T-cell and B-cell proliferation, facilitate the differentiation of naive CD4+ T cells into Treg cells, guide macrophages to adopt an immunosuppressive phenotype, and inhibit the generation of IgM and IgG. Additionally, MSCs induce T-cell apoptosis, subsequently prompting macrophages to release TGFβ, leading to the differentiation of Tregs and the establishment of immune tolerance [14].

3. Mechanisms of Action

3.1. Paracrine signaling

MSCs secrete a myriad of bioactive molecules, including cytokines, growth factors, and extracellular vesicles [18]. These factors influence the neighboring cells, modulating their behavior and contributing to the anticancer effects of MSC therapy [2].

3.2. Immunomodulation

MSCs interact with various immune cells, such as T cells, B cells, and natural killer cells, to modulate immune responses [19]. This immunomodulatory

effect creates an anti-inflammatory and antitumor microenvironment [20].

3.3. Differentiation potential

Under specific conditions, MSCs can differentiate into different cell types, offering the potential to replace damaged or cancerous cells [2]. This regenerative capacity adds an additional layer to the therapeutic potential of MSC therapy [21].

4. Challenges and Future Perspectives

Achieving consistent and reliable tumor tropism remains a challenge. Ensuring that MSCs effectively target and home in on diverse tumor types is crucial for the success of this therapy. Despite promising results in preclinical studies, concerns about the safety of MSC therapy persist. Rigorous clinical trials are essential to establish the safety profile and efficacy of MSCs in diverse cancer populations. Standardizing protocols for MSC isolation, expansion, and administration is critical for ensuring reproducibility and comparability across different studies.

5. Conclusion

MSC therapy represents a novel and promising approach in the fight against cancer. By leveraging their unique properties, MSCs contribute to targeted drug delivery, immune modulation, and the creation of a tumor-suppressive microenvironment. While challenges persist, ongoing research holds the potential to unlock the full therapeutic capabilities of MSCs, offering new hope for cancer patients worldwide.

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