Microenvironment: Key to Regeneration, Cancer, Therapy

Priya Mehta
Department of Cellular Pathophysiology, AIIMS, New Delhi, India

*Corresponding Authors**

Priya Mehta
Department of Cellular Pathophysiology, AIIMS, New Delhi, India
E-mail: priya.mehta@aiims.ac.in

Received: 01-Oct-2025; **Accepted:** 10-Nov-2025; **Published:** 10-Nov-2025

Introduction

The extracellular matrix (ECM) is more than just a scaffold; it's a dynamic participant in regulating stem cell behavior, crucial for regenerative medicine [1].

This review delves into how ECM composition and mechanics influence stem cell fate, offering insights for advanced tissue engineering strategies and therapeutic applications.

Building on this, engineering artificial stem cell niches offers a powerful approach to control stem cell behavior for regenerative applications [4].

Recent advances in designing biomaterials and microenvironmental cues aim to precisely modulate stem cell fate, providing a comprehensive overview of current strategies and future directions.

Creating optimal microenvironments is essential for successful regenerative medicine applications [6].

This involves exploring various strategies for microenvironmental engineering, including advanced biomaterials and cell-based approaches, to guide tissue regeneration and repair, addressing challenges and outlining future prospects.

Moving from regenerative applications, the tumor microenvironment (TME) presents a complex landscape critically involved in disease progression.

Tumor cells, along with their surrounding microenvironment, often undergo significant metabolic changes that fuel cancer progression [2].

Metabolic reprogramming in the TME can be targeted to develop novel therapeutic strategies for various cancers, highlighting critical pathways and potential drug candidates.

Immune cells within the tumor microenvironment exhibit remarkable plasticity, adapting their functions in response to various cues [3].

This review discusses the mechanisms driving immune cell plasticity and its profound implications for cancer immunotherapy, suggesting ways to manipulate these cells for better patient outcomes.

The physical forces and mechanical properties of the tumor microenvironment play a significant role in cancer progression and resistance to therapy [5].

This review summarizes current understanding of mechanobiology in the TME, identifying key mechanical cues and discussing opportunities for developing mechanotherapeutics.

Targeting the specific characteristics of the tumor microenvironment is a promising strategy for enhancing drug delivery and therapeutic efficacy [9].

Smart drug delivery systems are designed to interact with and respond to the unique features of the TME, improving drug accumulation and reducing systemic toxicity.

Single-cell sequencing technologies have revolutionized our ability to dissect the heterogeneity of the tumor microenvironment at unprecedented resolution [10].

This review discusses current challenges and highlights emerging opportunities for gaining deeper insights into cancer biology and identifying new therapeutic targets.

Beyond oncology, the microenvironment's influence extends to other critical physiological and pathological states.

Organ fibrosis involves complex interactions between resident cells and the extracellular matrix, leading to pathological tissue remodeling [7].

This article provides a detailed look at the cellular and ECM components that drive fibrotic processes across different organs, offering potential targets for therapeutic intervention.

The neurovascular unit, comprising various cell types and the ECM, forms a critical microenvironment for maintaining brain health [8].

This review discusses its dynamic role in neurological diseases, highlighting how dysregulation of this unit contributes to pathology and offers targets for therapeutic development.

Cite this article: Mehta P,(2025) Microenvironment: Key to Regeneration, Cancer, *Therapy. jmcb* 07: 171. DOI: 1037532.jmcb.2025.7.4.171

Description

The extracellular matrix (ECM) is far more than a simple scaffold; it acts as a dynamic participant in regulating stem cell behavior, which is fundamental for regenerative medicine. This area of study deeply explores how ECM composition and its mechanical properties influence stem cell fate, providing valuable insights for advanced tissue engineering strategies and therapeutic applications [1]. Extending this, engineering artificial stem cell niches represents a powerful method to precisely control stem cell behavior for various regenerative purposes. Recent progress in designing novel biomaterials and specific microenvironmental cues aims to modulate stem cell fate with high precision, giving us a thorough overview of current strategies and future directions in this evolving field [4].

Indeed, creating optimal microenvironments is paramount for the success of regenerative medicine applications. This involves a comprehensive exploration of diverse microenvironmental engineering strategies, including the use of advanced biomaterials and innovative cell-based approaches. The goal is to effectively guide tissue regeneration and repair, addressing existing challenges and sketching out future prospects for significant advancements [6]. Beyond regenerative contexts, these dynamic interactions are evident in diverse biological systems, underpinning both healthy function and disease states.

In the challenging domain of cancer, the tumor microenvironment (TME) is a crucial area of investigation. Tumor cells, alongside their surrounding microenvironment, frequently undergo profound metabolic changes that aggressively fuel cancer progression. Understanding this metabolic reprogramming in the TME is key, as it can be directly targeted to develop novel therapeutic strategies for a range of cancers, shedding light on critical pathways and identifying potential drug candidates [2]. Furthermore, immune cells situated within the TME demonstrate remarkable plasticity, adeptly adjusting their functions in response to various internal and external cues. This review illuminates the mechanisms driving immune cell plasticity and its significant implications for cancer immunotherapy, offering practical suggestions for manipulating these cells to achieve superior patient outcomes [3].

The physical forces and mechanical properties inherent in the tumor microenvironment also play a substantial role in cancer progression and contribute to resistance to therapy. Current research comprehensively summarizes the understanding of mechanobiology within the TME, pinpointing key mechanical cues and discussing opportunities for the development of mechanotherapeutics [5]. A promising strategy for enhancing drug delivery and therapeutic efficacy involves targeting the specific characteristics of the TME. This includes the development of smart drug delivery systems specifically designed to interact with and respond to the unique features of the tumor microenvironment, thereby improving drug accumulation at the tumor site and simultaneously reducing systemic toxicity [9].

To unravel the intricate heterogeneity of the tumor microenvironment with unprecedented resolution, single-cell sequencing technologies have emerged as revolutionary tools. This review explores the current challenges in applying these advanced technologies and highlights the burgeoning opportunities they present for gaining deeper insights into cancer biology, ultimately leading to the identification of new therapeutic targets [10]. Moving to other disease areas, organ fibrosis is characterized by complex interactions between resident cells and the extracellular matrix, which results in pathological tissue remodeling. This article offers a detailed examination of the cellular and ECM components that drive fibrotic processes across various organs, proposing potential targets for therapeutic intervention [7]. Similarly, the neurovascular unit, a complex structure comprising diverse cell types and the ECM, forms a critical microenvironment essential for maintaining optimal brain health. Its dynamic role in neurological diseases is a subject of active discussion, emphasizing how dysregulation within this unit contributes significantly to pathology and presents viable targets for therapeutic development [8].

Conclusion

The microenvironment plays a critical and dynamic role in various biological processes, ranging from regenerative medicine to cancer progression and neurological health. Research highlights the extracellular matrix (ECM) as a key regulator of stem cell behavior, where its composition and mechanics are vital for influencing stem cell fate, opening doors for advanced tissue engineering and therapeutic strategies. Beyond just a scaffold, the ECM actively participates in guiding regeneration. In oncology, the tumor microenvironment (TME) is a central focus, recognized for its significant metabolic changes that fuel cancer progression. Targeting metabolic reprogramming within the TME offers novel therapeutic avenues for various cancers. Immune cells within the TME also show remarkable plasticity, adapting their functions in response to diverse cues. Understanding these mechanisms is essential for improving cancer immunotherapy outcomes. Mechanical properties and physical forces within the TME similarly impact cancer progression and therapy resistance. Mechanobiology in this context identifies crucial mechanical cues, suggesting opportunities for developing mechanotherapeutics. Engineering these complex microenvironments, whether for stem cell niches or general regenerative applications, involves advanced biomaterials and cell-based approaches to guide tissue repair. This underscores the need for optimal microenvironments for successful regenerative medicine. Further investigations delve into specific microenvironments, such as the cellular and ECM components driving organ fibrosis, or the neurovascular unit's dynamic role in brain health and disease. The heterogeneity of the TME is also being dissected using single-cell sequencing technologies, revealing deeper insights into cancer biology and potential new therapeutic targets. Moreover, smart drug delivery systems are being developed to specifically interact with the TME, aiming to enhance drug efficacy and reduce systemic toxicity. Together, these studies emphasize the pervasive influence of the microenvironment on biological function and disease, offering multiple points for therapeutic intervention and engineering for health.

References

1. Nardone G, Peppas NA, Papanikolopoulou ME. The Extracellular Matrix: *A Dynamic Regulator of Stem Cell Fate and Function in Regenerative Medicine. Adv Healthc Mater.* 2023;12:2302307.

2. Liu Y, Zhao R, Wang W. Metabolic reprogramming in the tumor microenvironment: a target for cancer therapy. *J Exp Clin Cancer Res.* 2022;41:219.

3. Chen H, Li T, Zhang Y. Immune cell plasticity in the tumor microenvironment: mechanisms and therapeutic implications. *Signal Transduct Target Ther.* 2024;9:13.

Cite this article: Mehta P,(2025) Microenvironment: Key to Regeneration, Cancer, *Therapy. jmcb* 07: 171. DOI: 1037532.jmcb.2025.7.4.171

4. Kulkarni M, Bahl K, Sethu P. Stem Cell Niche Engineering: *Recent Advances and Future Perspectives. Adv Sci* (Weinh). 2023;10:2301980.

5. Zhang Y, Li M, Wang X. Mechanobiology of the tumor microenvironment: *Current understanding and therapeutic opportunities. Trends Cancer.* 2022;8:51-64.

6. Lee J, Park H, *Kim Y. Microenvironmental engineering for regenerative medicine. J Control Release.* 2021;331:31-48.

7. Kisseleva T, Brenner DA, *Trost C. The cellular and extracellular matrix microenvironment in organ fibrosis. J Clin Invest.* 2023;133:e172051.

8. Chen T, Zhang F, Lu Y. The neurovascular unit: *A dynamic cellular microenvironment in brain health and disease. Mol Neurodegener.* 2022;17:54.

9. Mura S, Kopeček J, *Torchilin VP. Smart drug delivery systems targeting the tumor microenvironment. J Control Release.* 2021;331:195-217.

10. Tirosh I, Regev A, Zhang J. Single-cell sequencing of the tumor microenvironment: challenges and opportunities. *Cell.* 2023;186:260-279.

Cite this article: Mehta P,(2025) Microenvironment: Key to Regeneration, Cancer, *Therapy. jmcb* 07: 171. DOI: 1037532.jmcb.2025.7.4.171