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REVIEW

Cancer cell plasticity: from cellular, molecular, and genetic mechanisms to tumor heterogeneity and drug resistance

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Abstract
Cancer is a complex disease displaying a variety of cell states and phenotypes. This diversity, known as cancer cell plasticity, confers cancer cells the ability to change in response to their environment, leading to increased tumor diversity and drug resistance. This review explores the intricate landscape of cancer cell plasticity, offering a deep dive into the cellular, molecular, and genetic mechanisms that underlie this phenomenon. Cancer cell plasticity is intertwined with processes such as epithelial-mesenchymal transition and the acquisition of stem cell–like features. These processes are pivotal in the development and progression of tumors, contributing to the multifaceted nature of cancer and the challenges associated with its treatment. Despite significant advancements in targeted therapies, cancer cell adaptability and subsequent therapy-induced resistance remain persistent obstacles in achieving consistent, successful cancer treatment outcomes. Our review delves into the array of mechanisms cancer cells exploit to maintain plasticity, including epigenetic modifications, alterations in signaling pathways, and environmental interactions. We discuss strategies to counteract cancer cell plasticity, such as targeting specific cellular pathways and employing combination therapies. These strategies promise to enhance the efficacy of cancer treatments and mitigate therapy resistance. In conclusion, this review offers a holistic, detailed exploration of cancer cell plasticity, aiming to bolster the understanding and approach toward tackling the challenges posed by tumor heterogeneity and drug resistance. As articulated in this review, the delineation of cellular, molecular, and genetic mechanisms underlying tumor heterogeneity and drug resistance seeks to contribute substantially to the progress in cancer therapeutics and the advancement of precision medicine, ultimately enhancing the prospects for effective cancer treatment and patient outcomes.

Keywords Cancer cell plasticity · Cancer stem cells · Epithelial-mesenchymal transition · Tumor heterogeneity · Drug resistance · Targeted therapies

1 Introduction

Cancer stands as one of the most formidable health challenges of our time, driven by the unrestrained growth and division of abnormal cells within the body. This unwarranted proliferation infiltrates and damages healthy tissues, culminating in a diverse spectrum of disorders, each identified by the cell or tissue type of origin. With a projected statistic that one in every four individuals over the age of 65 will have battled cancer by 2040, it is underscored as a leading global cause of death [1].

This multifaceted disease evolves through numerous steps, with many malignant pathways leading to diverse tumor types and subtypes. Each pathway includes unique aberrations and consequentially acquired traits necessary for overcoming tissue-specific barriers in specific tumorigenesis pathways [2, 3].

However, one critical aspect threading through this complexity is cancer cell plasticity. This phenomenon allows cancer cells to adapt and change, making them even more resilient and difficult to treat. Cancer cell plasticity is closely related to the epithelial-mesenchymal transition and the acquisition of stem cell features, both of which play significant roles in tumor development, diversity, and treatment resistance. Understanding this plasticity is crucial for

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