CHAPTER

Tumor microenvironment-mediated targeted drug delivery to breast cancer cells

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12.1 Introduction

As per a World Health Organization report in 2018, breast cancer is the second leading diagnosed cancer after lung cancer worldwide and the most common cancer in females [1], also being for the most common cause of death from cancer among women globally. Early-stage diagnosis may decrease the mortality rate significantly, but therapeutic possibilities are quite limited in advanced-stage breast cancer. Consequently, there is a need to understand better breast cancer's molecular determinants responsible for the initiation, progression, and resistance to therapy. The knowledge of molecular determinants may help in the development of molecular-targeted therapeutic options to treat breast cancer more effectively. In this way, one of the essential determinants, such as TME, plays a vital role in cancer progression, cell proliferation, immunosuppression, metastasis, invasion, and drug resistance to therapeutics [2]. The existing evidence suggests that the tumor consists of neoplastic cells and significantly changes around the stroma. The TME consists of mainly cellular and noncellular components, and the abnormal extracellular matrix (ECM) might provide suitable conditions for tumor growth, invasion, and metastasis. Both the cellular and noncellular TME components may impair anticancer treatment and develop drug resistance [2].

The cellular components of the TME of breast cancer consist of cells such as immune cells, endothelial cells, cancer-associated fibroblasts (CAFs), adipocytes, and lymphoid cells. The cells in the breast cancer microenvironment are distinguished by molecular abnormalities and aberrant signaling pathways. A variety of immune cells such as T helper-2 cells, neutrophils, tumor-associated macrophages (TAMs), and CD4+, allow tumor cells to survive, and metastasis promotes escape from destruction by immunosuppression [3,4]. Aberrant endothelial cell interactions with abnormal pericytes (irregular margins and cytoplasmic

Targeted Nanomedicine for Breast Cancer Therapy. DOI: https://doi.org/10.1016/B978-0-12-824476-0.00015-2