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Carcinoma Associated Mesenchymal Stem/Stromal Cells - Architects of the Pro-tumorigenic tumor microenvironment

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Free article

Abstract

The interaction between tumor cells and non-malignant hosts cells within the tumor microenvironment (TME) is critical to the pathophysiology of cancer. These non-malignant host cells, consisting of a variety of stromal, immune and endothelial cells, engage in a complex bidirectional crosstalk with the malignant tumor cells. Mesenchymal stem/stromal cells (MSCs) are one of these host cells, and they play a critical role in directing the formation and function of the entire TME. These MSCs are epigenetically reprogrammed by cancer cells to assume a strongly pro-tumorigenic phenotype and are referred to as carcinoma-associated mesenchymal stem/stromal cells (CA-MSCs). Studies over the last decade demonstrate that CA-MSCs not only directly interact with cancer cells to promote tumor growth and metastasis, but also orchestrate the formation of the TME. CA-MSCs can differentiate into virtually all stromal sub-lineages present in the TME, including pro-tumorigenic cancer associated fibroblasts (CAF), myofibroblasts, and adipocytes. CA-MSCs and the CAFs they produce, secrete much of the extracellular matrix in the TME. Furthermore, CA-MSC secreted factors promote angiogenesis, and recruit immunosuppressive myeloid cells effectively driving tumor immune exclusion. Thus CA-MSCs impact nearly every aspect of the TME. Despite their influence on cancer biology, as CA-MSCs represent a heterogenous population without a single definitive marker, significant confusion remains regarding the origin and proper identification CA-MSCs. This

review will focus on the impact of CA-MSCs on cancer progression and metastasis and the ongoing work on CA-MSC identification, nomenclature and mechanism of action.