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Deciphering the possible reciprocal loop between hepatic stellate cells and cancer cells in the tumor microenvironment of the liver

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Abstract

Activated hepatic stellate cells (HSCs)/myofibroblasts are the important sources of cancer-associated fibroblasts in the liver tumor microenvironment (TME). The crosstalk between activated HSCs and tumor cells mediates HCC progression, metastasis, tumor cell survival, angiogenesis and chemoresistance. In TME, HCC cells secrete various soluble factors responsible for the phenotypic activation of quiescent HSCs. Tumor cells use activated HSC-derived extracellular matrix (ECM) for migration and invasion. Further, in liver TME, activated HSCs and sinusoidal endothelial cells engage in a crosstalk that causes the secretion of angiogenesis and metastasis-related growth factors and cytokines. Activated HSCs and immune cells crosstalk to decrease immune surveillance in the liver TME by increasing the population of T regulatory cells and M2 macrophages or myeloid-derived suppressor cells. Thus, HSCs play a vital role in liver TME cell interactions. Therefore, a deep understanding of HSCs activation and their crosstalk with cancer and immune cells in TME may lead to the development of novel therapeutic strategies to target HCC. © 2023 Elsevier B.V.

Author Keywords

Extracellular matrix; Hepatocellular carcinoma; Liver fibrosis; Transforming growth factor

Index Keywords

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