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REVIEW

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Mesenchymal stromal cells induce inhibitory effects on hepatocellular carcinoma through various signaling pathways

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Abstract

Hepatocellular carcinoma (HCC) is the most prevalent type of malignant liver disease worldwide. Molecular changes in HCC collectively contribute to Wnt/β-catenin, as a tumor proliferative signaling pathway, toll-like receptors (TLRs), nuclear factor-kappa B (NF-κB), as well as the c-Jun NH2-terminal kinase (JNK), predominant signaling pathways linked to the release of tumor-promoting cytokines. It should also be noted that the Hippo signaling pathway plays an important role in organ size control, particularly in promoting tumorigenesis and HCC development. Nowadays, mesenchymal stromal cells (MSCs)-based therapies have been the subject of in vitro, in vivo, and clinical studies for liver such as cirrhosis, liver failure, and HCC. At present, despite the importance of basic molecular pathways of malignancies, limited information has been obtained on this background. Therefore, it can be difficult to determine the true concept of interactions between MSCs and tumor cells. What is known, these cells could migrate toward tumor sites so apply effects via paracrine interaction on HCC cells. For example, one of the inhibitory effects of MSCs is the overexpression of dickkopf-related protein 1 (DKK-1) as an important antagonist of the Wnt signaling pathway. A growing body of research challenging the therapeutic roles of MSCs through the secretion of various trophic factors in HCC. This review illustrates the complex behavior of MSCs and precisely how their inhibitory signals interface with HCC tumor cells.

Keywords: Mesenchymal stromal cells, Hepatocellular carcinoma, Wnt signaling, Toll like receptor, Nuclear factor-kappa B, JNK pathway

Introduction

Hepatocellular carcinoma (HCC) is the most common type of liver malignancy, occurs predominantly in patients with underlying chronic liver disease and cirrhosis [1]. Hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, combined with the advanced stage of liver fibrosis are thought to be the major risk factors for HCC [2].

There are alternative treatments available for this particular type of cancer, including chemotherapy with anti-cancer agents like sorafenib, radiotherapy, and immunotherapy, as well as the surgical resection of tumoral lesions. Ultimately, liver transplantation is an accepted modality of treatment in this background [3]. Although a liver transplant may offer the best chance of survival in patients with end-stage liver disease, the potential complications of this procedure lead to an urgent need to develop new treatment strategies for HCC. Cell therapy research propose some new mechanisms for tissue regeneration that would be used as a suitable replacement alone or in combination with other medications [4, 5].

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