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Effects of treatment with maraviroc a CCR5 inhibitor on a human hepatic stellate cell line

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After an acute liver damage, tissue regeneration repairs lesions with degradation of deposed fibrotic material, while mechanisms of tissue restoration are persistently activated following several repeated injuries, inducing deposition of extracellular matrix. (ECM).

Factors responsible for ECM remodeling have been identified in a pathway involving a family of zinc-dependent enzyme matrix metalloproteinases (MMPs), together with tissue inhibitor of metalloproteinases (TIMPs). Recent experimental models suggested a role of CCR5 receptor in the genesis of liver fibrosis. Drawing from these background we decided to evaluate the effects of the treatment with the CCR5 inhibitor Maraviroc on LX-2, a human hepatic stellate cell line (HSC). Treatment with Maraviroc resulted in a block in S phase of LX-2 cells with increased expression levels of cyclin D1 and p21 while the expression of p53 was reduced. Treatment with Maraviroc was also able to block the accumulation of fibrillar collagens and extracellular matrix proteins (ECM), as demonstrated by the decrease of specific markers as Collagen type I, α-SMA and TGF-β1. In addition we observed a down regulation of both metalloproteins (MMP-2, MMP-9), used for the degradation of the extracellular matrix and their inhibitors (TIMP-1, TIMP-2). The identification of a compound that may modulate the dynamic of liver fibrosis could be crucial in all chronic liver diseases. Maraviroc could play an important role because, in addition to its own anti-HIV activity, it could reduce the release of pro-inflammatory citokynes implicated in liver fibrogenesis.

Key words

Maraviroc, human hepatic stellate cell line, liver fibrosis.