Cholangiokines: undervalued modulators in the hepatic microenvironment

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Autoren

Xiurong Cai Frank Tacke Adrien Guillot

Hanyang Liu

Abstract

The biliary epithelial cells, also known as cholangiocytes, line the intra- and extrahepatic bile ducts, forming a barrier between intra- and extra-ductal environments. Cholangiocytes are mostly known to modulate bile composition and transportation. In hepatobiliary diseases, bile duct injury leads to drastic alterations in cholangiocyte phenotypes and their release of soluble mediators, which can vary depending on the original insult and cellular states (quiescence, senescence, or proliferation). The cholangiocyte-secreted cytokines (also termed cholangiokines) drive ductular cell proliferation, portal inflammation and fibrosis, and carcinogenesis. Hence, despite the previous consensus that cholangiocytes are bystanders in liver diseases, their diverse secretome plays critical roles in modulating the intrahepatic microenvironment. This review summarizes recent insights into the cholangiokines under both physiological and pathological conditions, especially as they occur during liver injury-regeneration, inflammation, fibrosis and malignant transformation processes.