Role of WISP1 in Stellate Cell Migration and Liver Fibrosis

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Abstract

The mechanisms underlying the remarkable capacity of the liver to regenerate are still not completely understood. Particularly, the cross-talk between cytokines and cellular components of the process is of utmost importance because they represent potential avenues for diagnostics and therapeutics. WNT1-inducible-signaling pathway protein 1 (WISP1) is a cytokine member of the CCN family, a family of proteins that play many different roles in liver pathophysiology. WISP1 also belongs to the earliest and strongest upregulated genes in mouse livers after CCl4 intoxication and has recently been shown to be secreted by tumor cells and to bind to type 1 collagen to cause its linearization in vitro and in tumor tissue in vivo. We show that WISP1 expression is strongly induced by TGFβ, a critical cytokine in wound healing processes. Additionally, secretion of WISP1 protein by hepatic stellate is increased in cells upon TGFβ stimulation (~seven-fold increase). Furthermore, WISP1 facilitates the migration of mouse hepatic stellate cells through collagen in vitro. However, in WISP1 knockout mice, no difference in stellate cell accumulation in damaged liver tissue and no influence on fibrosis was obtained, probably because the knockout of WISP1 was compensated by other factors in vivo.