Documents

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Hepatic stellate cell activation by TGFβ induces hedgehog signaling and endoplasmic reticulum stress simultaneously

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Abstract

Activation of hepatic stellates (HSCs) is known as the major cause of initiation and progression of liver fibrosis. A wide array of events occurs during HSC activation including induction of hedgehog (Hh) signaling and endoplasmic reticulum (ER) stress. Targeting HSC activation may provide promising insights into liver fibrosis treatment. In this regard, establishing in vitro models which can mimic the molecular pathways of interest is very important. We aimed to activate HSC in which Hh signaling and ER stress are stimulated simultaneously. We used 5 ng/ml TGFβ to activate LX-2 cells, HSC cell line. Gene expression analysis using qRT-PCR, immunostaining and immunoblotting were performed to show HSC activation associated markers. Furthermore, the migration capacity of the TGFβ treated cells is evaluated. The results demonstrated that major fibrogenic markers including collagen1a, lysyl oxidase, and tissue inhibitor of matrix metalloproteinase 1 genes are up-regulated significantly. In addition, our immunofluorescence and immunoblotting results showed that protein levels of GLI-2 and XBP1, were enhanced. Moreover, we found that TGFβ treatment reduced the migration of LX-2 cells. Our results are compatible with high throughput data analysis with respect to differentially expressed genes of activated HSC compared to the quiescent ones. Moreover, our findings suggest that quercetin can reduce fibrogenic markers of activated HSCs as well as osteopontin expression, a target gene of hedgehog signaling. © 2022

Author Keywords

Endoplasmic reticulum stress; Hedgehog signaling; Hepatic stellate cell activation; Liver fibrosis

Index Keywords

collagen type 1, collagen type 1a, osteopontin, protein lysine 6 oxidase, quercetin, tissue inhibitor of metalloproteinase 1, transforming growth factor beta, unclassified drug, X box binding protein 1, zinc finger protein GLI2, collagen, sonic hedgehog protein, transforming growth factor beta; antifibrotic activity, Article, cell activation, cell migration, concentration (parameter), controlled study, differential gene expression, drug targeting, endoplasmic reticulum stress, gene expression profiling, hedgehog signaling, hepatic stellate cell, high throughput analysis, human, human cell, immunoblotting, immunofluorescence, immunohistochemistry, in vitro study, liver fibrosis, protein expression, real time polymerase chain reaction, upregulation, cell line, cell motion, drug effect, gene expression, hepatic stellate cell, metabolism, physiology, signal transduction; Cell Line, Cell Movement, Collagen, Endoplasmic Reticulum Stress, Gene Expression, Hedgehog Proteins, Hepatic Stellate Cells, Humans, Quercetin, Signal Transduction, Transforming Growth Factor beta

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