TGF-β2 in Chronic Liver Disease and Hepatocellular Carcinoma

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BACKGROUND and AIMS

TGF-β is a prominent cytokine in diseased liver, orchestrating a complex cell-cell communication in wound healing and regeneration, inflammation, fibrogenesis as well as carcinogenesis. Although multiple preclinical approaches directed towards the prominent family member TGF-β1 provided promising results, none were successfully translated into clinics. We here demonstrate that TGF-β2 may represent an alternative therapeutic target in CLD and HCC.

METHODS

TGF-β1/2 expression, autocrine stimulation, Smad and non Smad signaling were performed in hepatic stellate cells (HSC), HCC cell lines and mouse models for chronic liver diseases, using real time PCR, immunoblotting, ELISAs and reporter assays.

RESULTS

In order to study TGF-β1 and TGF-β2 cytokine expression in different patients’ cohorts, data from 5 HCC patient cohorts (GEO database, GSE4975, GSE53056, GSE53576 and GSE53144 with a total number of 568 HCC patients with different etiologies, referred to independent normal liver samples and/or surrounding tissue samples were analyzed. The analysis of TGF-β1 and TGF-β2 expression in patients from different cohorts are displayed in scatter plots, representing each single patient. The GSE4975 cohort is composed of patients with different liver diseases, whereas the GSE53056 cohort is composed of children with CLD due to different etiologies, whereas the GSE53576 and GSE53144 cohorts are composed of patients, where the etiologies are significantly expressed in the Y-axis (p<0.05). Presented data shows the expression tendency in patients and allows further separation into clusters as well as correlation with clinical outcomes. The table displays the information colleted from the cohorts, that is mean fold change within the cohorts, expression tendency and number of patients showing this tendency.

CONCLUSIONS

Significant upregulation of TGF-β2 in line with TGF-β1 in CLD and HCC suggest TGF-β2 as promising therapeutic target to tackle fibrosis and HCC. Molecular details and specific outcome remain to be estimated further.

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