Organ-, inflammation- and cancer specific transcriptional fingerprints of pancreatic and hepatic stellate cells.

Abstract:
Tissue fibrosis is an integral component of chronic inflammatory (liver and pancreas) diseases and pancreatic cancer. Activated pancreatic- (PSC) and hepatic- (HSC) stellate cells play a key role in fibrogenesis. To identify organ- and disease-specific stellate cell transcriptional fingerprints, we employed genome-wide transcriptional analysis of primary human PSC and HSC isolated from patients with chronic inflammation or cancer. Stellate cells were isolated from patients with pancreatic ductal adenocarcinoma (n = 5), chronic pancreatitis (n = 6), liver cirrhosis (n = 5) and liver metastasis of pancreatic ductal adenocarcinoma (n = 6). Genome-wide transcriptional profiles of stellate cells were generated using our 51K human cDNA microarray platform. The identified organ- and disease specific genes were validated by quantitative RT-PCR, immunoblot, ELISA, immunocytochemistry and immunohistochemistry. Expression profiling identified 160 organ- and 89 disease- specific stellate cell transcripts. Collagen type 11a1 (COL11A1) was discovered as a novel PSC specific marker with up to 65-fold higher expression levels in PSC compared to HSC (p< 0.0001). Likewise, the expression of the cytokine CCL2 and the cell adhesion molecule VCAM1 were confined to HSC. PBX1 expression levels tend to
be increased in inflammatory- vs. tumor- stellate cells. Intriguingly, tyrosine kinase JAK2 and a member of cell contact-mediated communication CELSR3 were found to be selectively up-regulated in tumor stellate cells. We identified and validated HSC and PSC specific markers. Moreover, novel target genes of tumor- and inflammation associated stellate cells were discovered. Our data may be instrumental in developing new tailored organ- or disease-specific targeted therapies and stellate cell biomarkers.