Mononuclear cells modulate the activity of pancreatic stellate cells which in turn promote fibrosis and inflammation in chronic pancreatitis.

BACKGROUND: Interactions between mononuclear cells and activated pancreatic myofibroblasts (pancreatic stellate cells; PSC) may contribute to inflammation and fibrosis in chronic pancreatitis (CP). METHODS: Markers of fibrosis and inflammation were concomitantly analysed by immunohistochemistry in chronic pancreatitis tissues. In vitro, PSC were stimulated with TNFalpha and LPS. Primary human blood mononuclear cells (PBMC) and PSC were cocultured, followed by analysis of cytokines and extracellular matrix (ECM) proteins. PBMC were derived from healthy donors and CP and septic shock patients. RESULTS: In areas of mononuclear cell infiltration in chronic pancreatitis tissues, there was decreased immunoreactivity for collagen1 and fibronectin, in contrast to areas with sparse mononuclear cells, although PSC were detectable in both areas. LPS and TNFalpha induced collagen1 and fibronectin levels as well as the matrix degradation enzyme MMP-1. Coculture experiments with PSC and PBMC revealed increased fibronectin secretion induced by PBMC. In addition, donor and CP PBMC significantly induced an increase in IL-6, MCP-1 and TGFbeta levels under coculture conditions. Determination of the source of cytokines and ECM proteins by mRNA expression analysis confirmed PSC as...
major contributors of ECM production. The increase in cytokine expression was PBMC- and also PSC-derived. CONCLUSION: Mononuclear cells modulate the activity of pancreatic stellate cells, which may in turn promote fibrosis and inflammation.