Collagen type V promotes the malignant phenotype of pancreatic ductal adenocarcinoma.

Abstract:
Excessive matrix production by pancreatic stellate cells promotes local growth and metastasis of pancreatic ductal adenocarcinoma and provides a barrier for drug delivery. Collagen type V is a fibrillar, regulatory collagen up-regulated in the stroma of different malignant tumors. Here we show that collagen type V is expressed by pancreatic stellate cells in the stroma of pancreatic ductal adenocarcinoma and affects the malignant phenotype of various pancreatic cancer cell lines by promoting adhesion, migration and viability, also after treatment with chemotherapeutic drugs. Pharmacological and antibody-mediated inhibition of \( \beta 1 \)-integrin signaling abolishes collagen type V-induced effects on pancreatic cancer cells. Ablation of collagen type V secretion of pancreatic stellate cells by siRNA reduces invasion and proliferation of pancreatic cancer cells and tube formation of endothelial cells. Moreover, stable knock-down of collagen type V in pancreatic stellate cells reduces metastasis formation and angiogenesis in an orthotopic mouse model of ductal adenocarcinoma. In conclusion, paracrine loops involving cancer and stromal elements and mediated by collagen type V promote the malignant phenotype of pancreatic ductal adenocarcinoma and underline the
relevance of epithelial-stromal interactions in the progression of this aggressive neoplasm.

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