Syndecan-2 promotes perineural invasion and cooperates with K-ras to induce an invasive pancreatic cancer cell phenotype.

Abstract:
We have identified syndecan-2 as a protein potentially involved in perineural invasion of pancreatic adenocarcinoma (PDAC) cells. Syndecan-2 (SDC-2) expression was analyzed in human normal pancreas, chronic pancreatitis and PDAC tissues. Functional in vitro assays were carried out to determine its role in invasion, migration and signaling. SDC-2 was expressed in the majority of the tested pancreatic cancer cell lines while it was upregulated in nerve-invasive PDAC cell clones. There were 2 distinct expression patterns of SDC-2 in PDAC tissue samples: SDC-2 positivity in the cancer cell cytoplasm and a peritumoral expression. Though SDC-2 silencing (using specific siRNA oligonucleotides) did not affect anchorage-dependent growth, it significantly reduced cell motility and invasiveness in the pancreatic cancer cell lines T3M4 and Su8686. On the transcriptional level, migration-and invasion-associated genes were down-regulated following SDC-2 RNAi. Furthermore, SDC-2 silencing reduced K-ras activity, phosphorylation of Src and--further downstream--phosphorylation of ERK2 while levels of the putative SDC-2 signal transducer p120GAP remained unaltered. SDC-2 is a novel (perineural) invasion-associated gene in PDAC which cooperates with K-ras to induce a more invasive phenotype.