Loss of ONECUT1 expression in human pancreatic cancer cells.

ONECUT1 (HNF-6) is the prototype of a new class of homeodomain transcription factors, that controls the development of pancreatic ducts during mouse development. In the present study, the role of ONECUT1 and its targeted genes TCF2, PKHD1 and CYS1 was analyzed in human pancreatic ductal adenocarcinoma (PDAC). mRNA levels of ONECUT1, TCF2, PKHD1 and CYS1 were measured in pancreatic tissues and pancreatic cancer cell lines by quantitative reverse-transcriptase polymerase chain reaction (QRT-PCR). Protein expression of ONECUT1 and TCF2 was assessed in pancreatic tissues by immunohistochemistry. ONECUT1 was transfected into Panc-1 and T3M4 pancreatic cancer cells and its effects on anchorage-dependent and -independent growth as well as invasion and adhesion were analyzed. Median mRNA levels of ONECUT1, TCF2, PKHD1 and CYS1 were 7.7-, 2.0-, 5.7- and 3.8-fold higher in normal tissues than in PDAC tissues. ONECUT1 protein was expressed in normal acinar and ductal cells, but neither in the cancer cells of PDAC tissues nor in 7 of 8 cultured pancreatic cancer cell lines. There was a significant positive correlation between ONECUT1 and TCF2, CYS1, and PKHD1 mRNA levels in PDAC tissues. Transfection of ONECUT1 into pancreatic cancer cells resulted in up-regulation of the target gene TCF2, a reduction in invasiveness, but no change in adhesion or growth. In conclusion, ONECUT1 expression is
lost in pancreatic cancer cells, suggesting a tumor suppressor function in this malignancy.