Hypoxia-inducible proto-oncogene Pim-1 is a prognostic marker in pancreatic ductal adenocarcinoma.

BACKGROUND: Pim-1 is a proto-oncogene involved in cell survival, differentiation and proliferation in several hematologic and epithelial malignancies. Clinically, absence of Pim-1 expression correlates with poor prognosis in prostate cancer. In the present study, the expression of Pim-1 is analyzed in pancreatic cancer and correlated to clinicopathological parameters.

RESULTS: Compared to benign, inflammatory and pre-malignant conditions (i.e., the normal pancreas, chronic pancreatitis and benign intraductal papillary mucinous neoplasm), expression of Pim-1 mRNA and protein increased significantly in pancreatic malignancies. Absence of Pim-1 immunopositivity in cancer cells strongly correlated with a poor prognosis (median survival 13.8 vs. 23.4 months, p = 0.0016). In vitro, rapidly dividing (high versus low serum concentrations) and hypoxic cells displayed higher Pim-1 mRNA and protein levels. METHODS: Pim-1 mRNA and protein was evaluated with quantitative real-time RT-PCR, immunofluorescence and immunocytochemistry analyses. Ex vivo expression analysis using semi-quantitative immunohistochemistry was performed using human pancreatic tissues of the normal pancreas (n = 10), chronic pancreatitis (n = 30), pancreatic ductal adenocarcinoma (n = 59) and other pancreatic tumors (n = 42).
consecutive sections HIF1-alpha was used as a marker of hypoxia. Survival of patients (n = 35) was compared using the Kaplan-Meier method and a log-rank test. In vitro analyses were performed using cultured pancreatic cancer cell lines (n = 8) and primary human pancreatic stellate cells.

CONCLUSION: Hypoxia is a novel inducer of Pim-1 expression. Compared to non-malignant tissues Pim-1 significantly increases in pancreatic cancer. However, the presence of Pim-1 in cancer cells has a positive prognostic impact.