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Expression of Extracellular Matrix Metalloproteinase Inducer (EMMPRIN/CD147) in Pancreatic Neoplasm and Pancreatic Stellate Cells

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EMMPRIN (extracellular matrix metalloproteinase inducer, CD147) participates in the progression of various malignancies by stimulating the synthesis of specific matrix metalloproteinases (MMP) from peritumoral fibroblasts. In the present study, the expression and functional role of EMMPRIN was investigated in pancreatic neoplasm. QRT-PCR, immunohistochemistry, immunoblot, and ELISA analyses were used to analyze the expression, localization, and release of EMMRPIN. Silencing of EMMPRIN was performed using siRNA oligonucleotides, and functional consequences were assessed using growth assays, invasion assays, as well as MMP1/MMP2 and VEGF ELISA.

EMMPRIN mRNA levels were 2.2-fold increased in pancreatic cancer (n=52) and 2.0-3.5-fold increased in other pancreatic neoplasm (n=105), but unchanged in chronic pancreatitis (n=10) compared to normal pancreatic tissues (n=9). Strong and predominantly membranous immunostaining was observed in the cancer cells and surrounding stromal cells. EMMPRIN serum levels were also significantly increased in pancreatic cancer patients (n=44) (4.13 +/- 0.28 ng/ml) with an AUC of 0.97 compared to healthy volunteers (n=29) (0.95 +/- 0.16 ng/ml; $p<0.0001$) and with an AUC of 0.74 compared to chronic pancreatitis patients (n=20) (2.98 +/-0.5ng/ml; $p=0.0021$). EMMPRIN silencing did not significantly affect anchorage-dependent or -independent growth of pancreatic cancer cells. In contrast, EMMPRIN silencing in pancreatic stellate cells slightly repressed VEGF and MMP2 levels but strongly increased pro-MMP1 expression under co-culture conditions.

In conclusion, Increased EMMPRIN expression is present in different pancreatic neoplasm, likely representing a tumor-specific reaction with the potential to modulate the tumor microenvironment rather than a mere reflection of an activated stroma.