

MMP9 and S100A9 Expression in Peripheral Blood Mononuclear Cells (PBMC) Are Correlated with Pancreatic Adenocarcinoma (PDAC) and with PDAC-Associated Diabetes Mellitus

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Context Tumor-stroma-endocrine interactions favour pancreatic adenocarcinoma (PDAC) growth/progression and PDAC-associated diabetes mellitus (DM). S100A8/A9 and the matrix metalloproteinases (MMPs) 8 and 9 are overexpressed in PDAC stroma. **Objective** To verify whether S100A8, S100A9, MMP8 and MMP9 mRNA in peripheral blood mononuclear cells (PBMC) is useful for diagnosing and staging PDAC and/or for detecting PDAC-associated DM. To study the impact of S100A8/A9 and of PDAC-associated growth factors and cytokines on MMPs expression. **Methods** S100A8, S100A9, MMP8 e MMP9 mRNA were quantified by qRT-PCR in 62 PDAC, 37 chronic pancreatitis, 23 pancreatobiliary tract tumors (PBT) and 30 healthy controls (HC). PBMC (blood donors) were treated with insulin, EGF, TGFb1, S100A8/A9 before MMP8 and MMP9 mRNA analysis. **Results:** MMP8 and MMP9 were higher in PDAC and in PBT than in HC (Kruskal-Wallis test: $P < 0.0001$). S100A8 ($P = 0.902$) and S100A9 ($P = 0.303$) did not vary.

PDAC stage was not correlated with any molecule. At binary logistic regression analysis (PDAC presence or absence as dependent; S100A8, S100A9, MMP8, MMP9, age, gender, CA 19-9, bilirubin, glucose, C-peptide, CRP, and ALT as predictors), only MMP9 (OR=0.69; 95% CI: 0.48-0.99; $P = 0.047$) and CA 19-9 (OR=1.74; 95% CI: 1.31-2.33; $P = 0.0002$) were independently correlated with PDAC. In PDAC, DM was independently correlated only with S100A9 (OR=8.16; 95% CI: 2.31-28.78; $P = 0.001$) and age (OR=1.10; 95% CI: 1.01-1.21; $P = 0.028$). Insulin, EGF and TGFb1 did not affect MMP8 or MMP9 expression. S100A8/A9 significantly induced MMP8 ($F = 23.68$; $P = 0.002$) and MMP9 ($F = 93.84$; $P < 0.0001$) mRNA in PBMC. **Conclusion** PDAC is associated with an increased MMP9, while PDAC-associated DM is associated with an increased S100A9 expression in PBMC. S100A8/A9 effects on MMPs support the hypothesis of an intriguing relationship between inflammation, diabetes and PDAC.