Mucin (Muc) expression during pancreatic cancer progression in spontaneous mouse model: potential implications for diagnosis and therapy. [1]

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Abstract	**BACKGROUND:** Pancreatic cancer (PC) is a lethal malignancy primarily driven by activated Kras mutations and characterized by the deregulation of several genes including mucins. Previous studies on mucins have identified their significant role in both benign and malignant human diseases including PC progression and metastasis. However, the initiation of MUC expression during PC remains unknown because of lack of early stage tumor tissues from PC patients. **METHODS:** In the present study, we have evaluated stage specific expression patterns of mucins during mouse PC progression in (Kras(G12D);Pdx1-Cre (KC)) murine PC model from pancreatic intraepithelial neoplasia (PanIN) to pancreatic ductal adenocarcinoma (PDAC) by immunohistochemistry and quantitative real-time PCR. **RESULTS:** In agreement with previous studies on human PC, we observed a progressive increase in the expression of mucins particularly Muc1, Muc4 and Muc5AC in the pancreas of KC (as early as PanIN I) mice with advancement of PanIN lesions and PDAC both at mRNA and protein levels. Additionally, mucin expression correlated with the increased expression of inflammatory cytokines IFN-? ($p < 0.0062$), CXCL1 ($p < 0.00014$) and CXCL2 ($p < 0.08$) in the pancreas of KC mice, which are known to induce mucin expression. Further, we also observed progressive increase in inflammation in pancreas of KC mice from 10 to 50 weeks of age as indicated by the increase in the macrophage infiltration. Overall, this study corroborates with previous human studies that indicated the aberrant overexpression of MUC1, MUC4 and MUC5AC mucins during the progression of PC. **CONCLUSIONS:** Our study reinforces the potential utility of the KC murine model for determining the functional role of mucins in PC pathogenesis by crossing KC mice with corresponding mucin knockout mice and evaluating mucin based diagnostic and therapeutic approaches for lethal PC.
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