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Aberrant glycosylation on MUC5AC and MUC1 mucins as potential pancreatic cancer biomarkers

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Pancreatic adenocarcinoma (PDAC), the most common among pancreatic cancers, is nowadays the third cause of death by cancer in developed countries despite its low incidence, presenting a five-year survival rate of just 8%. Its high aggressiveness and the lack of biomarkers that allow for its diagnosis with enough sensibility and specificity explain this so unfavourable prognostic. Currently, the most used biomarker is CA19-9, but its levels are also altered in other tumours and benign pancreatic pathologies, reason why it is not useful for PDAC diagnosis due to lack of specificity. Thus, the search for novel biomarkers is an issue of concern for the scientific community.

During PDAC tumour transformation process, as in other cancers, the deregulated expression of various proteins has been described. In addition, aberrant glycosylation patterns have been detected on tumour cells. Hence, the combined analysis of glycoprotein over- or neo-expression and its carbohydrate epitopes could provide novel biomarkers for pancreatic cancer with enhanced specificity and sensibility. Mucins are a well characterised family of glycoproteins that can carry aberrant glycosylation in cancer, and so the main candidates of our study.

Our objective was to identify cancer-related glycan epitopes on MUC1 and MUC5AC mucins in PDAC as potential biomarkers. We have analysed the tumour-associated carbohydrate antigens sialyl-Lewis x (SLe^x) and sialyl-Tn (STn) on MUC1 and MUC5AC in PDAC tissues by IHC. The selected cohort for this study consisted of twenty-one PDAC tissues positive for SLe^x antigen and three normal pancreas specimens as controls. STn expression was shown in 76% of the PDAC tissues. MUC1 and MUC5AC were detected in 90% of PDAC tissues. We performed *in situ* proximity ligation assay combining antibodies against mucins and glycan epitopes to identify specific mucin glycoforms. MUC1-SLe^x and MUC5AC-SLe^x were found in 68% and 84% respectively, of the mucin expressing PDAC tissues, while STn hardly colocalized with any of the evaluated mucins. Further analysis by Western blot of MUC5AC and SLe^x in eight PDAC tissue lysates showed that six out of eight cases were positive for both markers. Moreover, immunoprecipitation of MUC5AC from positive PDAC tissues and subsequent SLe^x immunodetection confirmed the presence of SLe^x on MUC5AC. Altogether, MUC5AC-SLe^x glycoform is present in PDAC and can be regarded as a potential biomarker.