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MALDI-TOF/MS Biomarkers Discovery for Pancreatic Cancer Diagnosis: Emerging Role of Apolipoprotein A1 and Complement C3

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Context New serum biomarkers are needed for pancreatic cancer (PCa) diagnosis especially among patients with diabetes mellitus (DM), a risk factor for and a consequence of PCa. **Objective** To validate new serum biomarkers identified by MALDI-TOF/MS for PCa diagnosis. **Methods** MALDI-TOF/MS analysis was performed in sera from 22 controls, 51 PCa, 37 chronic pancreatitis (ChrPa), 24 DM, 29 gastric cancer (GC), and 24 chronic gastritis (CG). **Results** Eleven out of 160 selected features (m/z range 1,200-5,000) were highly correlated with pancreatic diseases (univariate and binary recursive partitioning tree analyses). By MALDI-TOF-TOF analysis three features (1,530, 1,550, 1,778 m/z) were found to be part of clusterin, human apolipoprotein A1 (Apo-A1), and human complement C3, respectively. Apo-A1 and C3 were measured in 172/187 sera and in an additional series of 69 new samples yielding 30 controls, 81 PCa, 26 ChrPa, 51 DM, 32 GC, 21 CG. Apo-A1 was reduced in PCa and in GC ($F=10.49$, $P<0.0001$). In 22/81 (27.2%) PCa and in 2/32 (6.2%) GC Apo-A1 values were below 0.6 g/L, while values in this order of magnitude were never found in the other groups (100% specificity). Apo-A1, C3 and CA 19-9 were correlated with PCa diagnosis at univariate logistic regression analysis; at multivariate logistic regression only Apo-A1 (OR=0.38, 95% CI=0.17-0.86, P=0.020) and C3 (OR=4.75, 95% CI=2.33-9.67, $P<0.001$) were confirmed to be strictly correlated with PCa. **Conclusion** Reduced serum levels of the anti-inflammatory and antioxidant protein Apo-A1, major protein in HDL, and increased serum levels of the inflammatory mediator C3 are potential biomarkers for PCa.