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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.