

TOWARDS TAILORED THERAPY FOR PANCREATIC CANCER

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BACKGROUND: Current methods of preoperative staging and predicting outcome following pancreatectomy for pancreatic cancer are inadequate. We evaluated the utility of multiple biomarkers from distinct biological pathways as predictive markers of response to pancreatectomy and patient survival.

METHODS: We assessed the relationship of 17 candidate biomarkers known, or suspected, to be aberrantly expressed in pancreatic cancer, with disease specific survival and response to therapy in a cohort of 601 patients. The candidate biomarkers examined were: transcriptional regulators - HOXB2 and LMO4; S100 calcium-binding proteins - S100A2, S100A6 and S100P; regulators of cell cycle progression - cyclins D1 and E1, p21^{WAF1/CIP1}, p27^{KIP1}, p16^{INK4A} and p53; cell membrane receptors - EGFR and RAI3; and signaling molecules - DPC4/Smad4, CRBP1, β -catenin and sFRP4.

RESULTS: Of the 17 candidate biomarkers examined, only elevated expression of S100A2 was an independent predictor of survival in both the training (n = 162), and validation sets (n = 439, HR 2.19, 95%CI: 1.48 – 3.25; p < 0.0001) when assessed in a multivariate model with clinical variables. Of significance, patients with high S100A2 expressing tumors had no survival benefit with pancreatectomy compared with those of equivalent stage who did not undergo resection, whereas those without high S100A2 expression had a survival advantage of 10.6 months (19.4 Vs 8.8 months, p < 0.0001) and a HR = 3.23 (95%CI: 2.39 – 4.33; p < 0.0001).

CONCLUSIONS: S100A2 expression is the best predictor of response to pancreatectomy for pancreatic cancer reported to date, and high S100A2 expression may represent the presence of occult metastatic disease at the time of surgery. Prospective measurement of S100A2 expression in diagnostic biopsies has potential clinical utility as a predictive marker of response to pancreatectomy.