

Prediction of survival and response to adjuvant therapy in pancreatic cancer

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Despite all efforts, patients with pancreatic ductal adenocarcinoma (PDAC) have a poor prognosis. Currently, adjuvant therapy provides a modest increase in median survival time of two to six months. New approaches are needed to individualize therapy based on molecular prognostic signatures to further improve patient survival.

In a multicentre study, gene expression profiles were analyzed from freshly frozen samples from 30 patients who underwent surgical resection of PDAC, and a network based approach to identify genes prognostic for survival was devised. The prognostic genes were validated using quantitative RT-PCR and immunohistochemistry on an independent set of 412 formalin-fixed, paraffin-embedded PDAC samples. Signature classifiers were created using support vector machine-based learning, and their accuracy was assessed with Monte Carlo cross-validation.

Our approach identified seven candidate marker genes prognostic for overall survival. Based on immunohistochemical staining for these markers, we developed signatures to predict the survival of patients with and without adjuvant therapy. Both signatures were independently predictive of survival and superior to established clinical prognostic factors such as grade, tumor size, and nodal status. The first signature (six genes) identifies a high and a low risk group after resection followed by adjuvant therapy (hazard ratio [HR] = 2.0, $p = 0.001$). The second signature (five genes) identifies a high and a low risk group after resection without adjuvant therapy (HR = 1.53, $p = 0.009$). For both signatures, the difference in median survival between the identified risk groups was five months.

We present a genome-wide screen for gene expression markers for predicting survival after resection in pancreatic cancer patients. Accurate predictors of outcome and response to adjuvant therapy can be used to personalize and thereby improve therapy.

Biography

Prof. Grützmann has completed his medical studies at the Charite (Berlin, Germany). He then became a qualified general surgeon with subsequent qualification in pancreatic surgery. His scientific interest is the molecular basis of pancreatic cancer. He has published more than 60 papers and book chapters. He is leader of the pancreatic surgery at the University hospital Carl Gustav Carus Dresden, Germany and leader of the pancreatic cancer laboratory at the same University hospital.