Reduced ?-dystroglycan expression correlates with shortened patient survival in pancreatic cancer.

Abstract:
Deregulation of cell-matrix interactions is considered an important factor in malignant transformation. Dystroglycan forms the interface between the basement membrane and the cell membrane in epithelia by its two subunits, ?- and ?-dystroglycan. Aberrant expression of dystroglycan has been observed in various human cancers. Here we assessed the expression of dystroglycan in pancreatic ductal adenocarcinoma (PDAC) and analyzed its association with clinical parameters. mRNA levels of dystroglycan were determined by real-time quantitative PCR in tissue samples from 60 patients with PDAC, from 48 patients with CP, and from 18 healthy donors. Furthermore, pancreatic cancer specimens of 53 patients were analyzed by immunohistochemistry using specific ?- and ?-dystroglycan antibodies. The staining was semiquantitatively evaluated and correlated to patient survival using the Kaplan-Meier method. On the mRNA level, dystroglycan was down-regulated in PDAC compared with the normal pancreas. In normal pancreatic tissues, ?- and ?-dystroglycans were mainly expressed on the basolateral cell membrane of acinar and ductal cells, while islet cells showed a cytoplasmatic staining. In contrast, in PDAC tissues, this membrane staining pattern was lost and replaced by a cytoplasmatic staining, suggesting impairments in the membrane translocation of both dystroglycans. Semiquantitative analysis revealed a
significant inverse correlation of ?- (but not ?-) dystroglycan staining and postoperative survival (P=0.039). Reduced expression and altered localization of dystroglycan is common in PDAC, potentially contributing to the aggressive behavior of this disease.