Abstract:

Cell-cell adhesion is a major factor in integrity of epithelia which is frequently disturbed in cancer leading to local invasion and distant metastasis. To define expression and function of activated leukocyte cell adhesion molecule (ALCAM, CD166) in pancreatic cancer and in pancreatic neuroendocrine tumors (PNET), microarray analyses, RT-PCR, immunohistochemistry, RNAi, adhesion, migration, invasion, and chemoresistance assays were used. We demonstrate that expression of ALCAM is altered and its serum levels are increased in pancreatic ductal adenocarcinoma (PDAC). ALCAM was expressed on the membranes of islet cells in the normal pancreas whereas normal pancreatic ducts were ALCAM-negative. In PDAC, ALCAM expression was generally rare though in some tumors, membranous, or cytoplasmic ALCAM was found. PNET were mostly ALCAM-positive with a cytoplasmic staining pattern which was in contrast to the membrane expression observed in non-transformed islet cells. In vitro, ALCAM silencing using RNAi had no effects on growth or invasion of pancreatic cancer cells but reduced cell adhesion and induced chemoresistance. In neuroendocrine tumor cell lines, silencing of ALCAM decreased cell growth. We propose ALCAM as a novel serum biomarker in human pancreatic tumors which is associated with cell adhesion, growth and chemoresistance.