Tenascin-C Enhances Pancreatic Cancer Cell Growth and Motility and Affects Cell Adhesion through Activation of the Integrin Pathway.

Abstract:
Pancreatic cancer (PDAC) is characterized by an abundant fibrous tissue rich in Tenascin-C (TNC), a large ECM glycoprotein mainly synthesized by pancreatic stellate cells (PSCs). In human pancreatic tissues, TNC expression increases in the progression from low-grade precursor lesions to invasive cancer. Aim of this study was the functional characterization of the effects of TNC on biologic relevant properties of pancreatic cancer cells. Proliferation, migration and adhesion assays were performed on pancreatic cancer cell lines treated with TNC or grown on a TNC-rich matrix. Stable transfectants expressing the large TNC splice variant were generated to test the effects of endogenous TNC. TNC-dependent integrin signaling was investigated by immunoblotting, immunofluorescence and pharmacological inhibition. Endogenous TNC promoted pancreatic cancer cell growth and migration. A TNC-rich matrix also enhanced migration as well as the adhesion to the uncoated growth surface of poorly differentiated cell lines. In contrast, adhesion to fibronectin was significantly decreased in the presence of TNC. The effects of TNC on cell adhesion were paralleled by changes in the activation state of paxillin and Akt. TNC affects proliferation, migration and adhesion of poorly differentiated pancreatic cancer cell lines and might therefore...
play a role in PDAC spreading and metastasis in vivo.

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