Dokumenttyp: journal article

Autor(en) des Beitrags:
Sperveslage, J; Frank, S; Heneweer, C; Egberts, J; Schniewind, B; Buchholz, M; Bergmann, F; Giese, N; Munding, J; Hahn, S; Kalthoff, H; Klöppel, G; Sipos, B

Titel des Beitrags:
Lack of CCR7 expression is rate limiting for lymphatic spread of pancreatic ductal adenocarcinoma.

Abstract:
CCR7 expression on tumor cells promotes lymphatic spread in several malignant tumors. However, a comprehensive characterization of the CCL19/CCL21-CCR7 axis in pancreatic ductal adenocarcinoma (PDAC), which is known for its high rates of lymph-node metastases, is still lacking. CCR7 mRNA and CCR7 protein were found to be expressed in spheroid cultures of all six examined PDAC cell lines. In migration assays, CCR7 expressing PDAC cells showed enhanced migration toward CCL19 and CCL21, the two ligands of CCR7. In an orthotopic nude mouse model, CCR7-transfected PT45P1 cells gave rise to significantly larger tumors and showed a higher frequency of lymph vessel invasion and lymph-node metastases than mock-transfected cells. In an analysis using quantitative real-time PCR, CCR7 showed fourfold overexpression in microdissected PDAC cells compared to normal duct cells. Moderate-to-strong immunohistochemical CCR7 expression, found in 58 of 121 well-characterized human PDACs, correlated with high rates of lymph vessel invasion. Conversely, PDACs completely lacking CCR7 expression showed only low rates of lymph vessel invasion and lymph-node metastases. The evaluation of CCL21 expression by immunofluorescence staining revealed a significant upregulation of CCL21 in perilumoral and intratumoral...
lymph vessels compared to lymph vessels in disease-free pancreata. In conclusion, our study revealed strong evidence that lack of CCR7 impairs the metastatic potential of PDAC. Lymph vessel invasion by CCR7 expressing PDAC cells may be additionally enhanced by upregulation of CCL21 in tumor-associated lymph vessels, representing a previously unknown factor of lymphatic spread.