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Titel des Beitrags:
TLR7 and TLR8 expression increases tumor cell proliferation and promotes chemoresistance in human pancreatic cancer.

Abstract:
Chronic inflammation as an important epigenetic and environmental factor for putative tumorigenesis and tumor progression may be associated with specific activation of Toll-like receptors (TLR). Recently, carcinogenesis has been suggested to be dependent on TLR7 signaling. In the present study, we determined the role of both TLR7 and TLR8 expression and signaling in tumor cell proliferation and chemoresistance in pancreatic cancer. Expression of TLR7/TLR8 in UICC stage I-IV pancreatic cancer, chronic pancreatitis, normal pancreatic tissue and human pancreatic (PANC1) cancer cell line was examined. For in vitro/in vivo studies TLR7/TLR8 overexpressing PANC1 cell lines were generated and analyzed for effects of (un-)stimulated TLR expression on tumor cell proliferation and chemoresistance. TLR expression was increased in pancreatic cancer, with stage-dependent upregulation in advanced tumors, compared to earlier stages and chronic pancreatitis. Stimulation of TLR7/TLR8 overexpressing PANC1 cells resulted in elevated NF-κB and COX-2 expression, increased cancer cell proliferation and reduced chemosensitivity. More importantly, TLR7/TLR8 expression increased
tumor growth in vivo. Our data demonstrate a stage-dependent upregulation of both TLR7 and TLR8 expression in pancreatic cancer. Functional analysis in human pancreatic cancer cells point to a significant role of both TLRs in chronic inflammation-mediated TLR7/TLR8 signaling leading to tumor cell proliferation and chemoresistance.