Toll like receptors promote auto regulative tumor cell growth and growth factor expression in pancreatic cancer

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Statement of the Problem: Toll like receptor (TLR) signaling has been suggested to play an important role in the inflammatory microenvironment of solid tumors and through this inflammation-mediated tumor growth. Recently we reported about the role of the two intracellularly expressed TLRs, TLR7 and TLR8, in solid tumor growth. Expression of both receptors is upregulated in primary tumors from patients with colon and pancreatic cancer. In both human cancers TLR 7 and 8 expressions was related rather to cancer cells then to tumor-infiltrating immune cells and their expression was associated with tumor cell growth and progression in both tumor entities. Here, we studied the role of tumor cells in their process of self-maintaining TLR expression independent of inflammatory cells and cytokine milieu for auto-regulative tumor growth signaling in pancreatic cancer.

Methodology & Theoretical Orientation: We analyzed the expression of TLR2, TLR4, and TLR9 in primary human cancers obtained from surgically resected patients and the impact of the TLRs on tumor growth via induced activation in several established pancreatic cancers. TLR-stimulated pancreatic cancer cells were specifically investigated for activated signaling pathways of VEGF/PDGF and anti-apoptotic Bcl-xL expression as well as tumor cell growth.

Findings: The primary pancreatic cancer tissues and cell lines expressed TLR 2, 4, and 9. TLR-specific stimulation resulted in activated MAP-kinase signaling, most likely via autoregulative stimulation of demonstrated TLR-induced VEGF and PDGF expression. Moreover, TLR activation prompted the expression of Bcl-xL and has been demonstrated for the first time to induce tumor cell proliferation in pancreatic cancer.

Conclusion & Significance: These findings strongly suggest that pancreatic cancer cells use specific Toll like receptor signaling to promote tumor cell proliferation and emphasize the particular role of TLR2, TLR4, and TLR9 in this autoregulative process of tumor cell activation and proliferation in pancreatic cancer.

Biography

Martin Gasser has his expertise in surgical oncology and clinical and experimental oncology of gastrointestinal malignancies. His research is focused on the influence of inflammation-induced tumorigenesis and tumor progression in colorectal and pancreatic cancer. In addition, he is interested in the role of cancer stem cells and the development of specific cancer cell-targeted as well as immune cell based-tumor therapies.

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