

Results: Our data in combination with the literature data showed that MMP-2, -7, -9, -12, -14, -15, and -25 are expressionally correlated with the tumor grade. The data for MMP-1, -11, -19 and -24 are contradictory, since some studies, including our own, suggest involvement during brain tumor development, whereas the results of other groups deny such connection. The remaining MMPs do not seem to play a major role during glioblastoma development, because they are either constitutively expressed or not expressed at all.

Conclusion: This is the first complete compilation of expression of all 23 human MMPs by astrocytic tumors. Specific MMP expression patterns may mark tumor aggressiveness. Expression studies will extend our understanding of tumor invasiveness and help us to find more effective therapeutic means for treatment of glioblastomas.

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P8. THE SERINE PROTEASE Bssp REGULATES KERATINOCYTE PROLIFERATION AND MIGRATION BY MODULATION OF E-CADHERIN/ β -CATENIN SIGNALLING

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Background: Carcinogenesis is a multistage process driven by genetic and epigenetic alterations that are associated with changes in the expression or function of oncogenes and tumor-suppressor genes.

Methods: In order to identify novel tumor-associated genes, we performed global gene expression profiling with specimens of a well-established multistage tumor model of mouse skin resulting in a comprehensive list of differentially expressed genes.

Results: One of these genes encodes for the secreted serine protease Bssp and is characterized by elevated expression in advanced stages of mouse skin tumors. Moreover, we found enhanced levels of kallikrein 6, the human homolog, in malignant squamous skin tumors of human patients as well as in tumors of other epithelial tissues suggesting a common role in carcinogenesis. To unravel the consequence of elevated Bssp expression in epithelial cells, we established stable transfected keratinocytes expressing exogenous Bssp. These cells displayed increased proliferation and advanced migration accompanied by impaired E-cadherin-mediated cell-cell adhesion and increased nuclear β -catenin localization. Enhanced proliferation of keratinocytes was confirmed in a wound healing experiment using a transgenic mouse model with exogenous Bssp expression in skin.

Conclusion: In summary our data imply that elevated Bssp/Klk6 levels support epithelial neoplasia due to modulation of E-cadherin/ β -catenin signalling and thereby facilitate proliferation and migration of tumor cells.

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P9. Eps8 ASSOCIATES WITH ACTIN AT THE LEADING EDGE AND INDICATES MIGRATORY POTENTIAL IN PANCREATIC CANCER CELL LINES

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Background: Pancreatic carcinoma is characterized by early metastasis. Increased cell motility is critical for metastasis of tumor cells. Cell motility is based on reorganization of the actin cytoskeleton in lamellipodia at the leading cell edge. Rac is a Rho-family small GTPase, which regulates rearrangement of the actin network and is also involved in tumor metastasis. Eps8, originally identified as a substrate of the epidermal growth factor receptor (EGFR), serves as a Rac guanine nucleotide exchange factor thus activating Rac. Eps8 is involved in cancer cell invasiveness and motility in fibrosarcoma cells. Eps8 further binds actin directly and possess barbed end capping activity.

Methods: Pancreatic tissue was obtained from patients that underwent pancreatic resection at the University of Heidelberg. Eight pancreatic cancer cell lines were used: AsPc-1, BxPC3, Capan1, Colo357, Miapaca, Panc1, Su8686, and T3M4. QRT-PCR was performed with the Light Cycler Fast Start DNA SYBR Green Kit. Immunofluorescence of EGFR-GFP, actin and Eps8 was analysed by confocal microscopy. Cell motility was quantified by the phagokinetic assay.

Results: QRT-PCR reveals that Eps8 expression is 4-fold increased in pancreatic carcinoma compared to normal pancreatic tissue. In pancreatic tissue, Eps8 is located apically in ductal epithelial cells. In all eight pancreatic cell lines analysed, Eps8-expression correlates with staging of the original tumors: cells derived from ascites exhibit the strongest Eps8 expression, followed by cells from metastases and primary tumors. In parallel, Eps8 expression in cell lines is associated with increased cancer cell motility. Subcellularly, Eps8 does not colocalize with the EGFR but is located at the tip of actin filaments and at the leading cell edge.

Conclusion: Eps8 is increased in pancreatic cancer. Association with dynamic actin at the leading cell edge in pancreatic cancer cell lines seems to be an important mechanism for pancreatic cancer cell migration promoting metastasis.

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P10. EFFECTS OF BONE SIALOPROTEIN ON PANCREATIC CANCER CELL GROWTH, INVASION AND METASTASIS

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Background: Bone sialoprotein (BSP); an acidic glycoprotein that plays a role in cancer cell growth, migration and invasion.

Methods: The expression, localisation and function of BSP in chronic pancreatitis (CP) and pancreatic ductal adeno-carcinoma