(PDAC) were analyzed by QRT-PCR, laser capture microdissection, DNA microarray analysis, immunoblotting, radioimmunoassay, immunohistochemistry, cell growth, invasion, scattering, and adhesion assays.

Results: BSP mRNA was detected in 40.7% of normal, in 80% of CP and in 86.4% of PDAC samples. The median BSP mRNA levels were 6.1 and 0.9 and zero copies/μl cDNA in PDAC, CP and normal pancreatic tissues, respectively. BSP was localized in the cytoplasm of the tubular complexes of CP and PDAC, and in pancreatic cancer cells. Five out of eight pancreatic cancer cell lines expressed BSP mRNA. Recombinant BSP (rBSP) inhibited Capan-1 and SU8686 pancreatic cancer cell growth, with a maximal effect of $-46.4 \pm 12.0\%$ in Capan-1 cells and $-45.7 \pm 14.5\%$ in SU8686 cells. rBSP decreased the invasion of SU8686 cells by $-59.1 \pm 11.2\%$ and of Capan-1 cells by $-13.3 \pm 3.8\%$ ($p < 0.05$), whereas it did not affect scattering or adhesion of both cell lines.

Conclusion: Endogenous BSP expression levels in pancreatic cancer cells and low to absent BSP expression in the surrounding stromal tissue elements may indirectly enhance the proliferation and invasion of pancreatic cancer cells.

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P11. INFLUENCE OF NEUROENDOCRINE TUMOR DIFFERENTIATION ON CELL ADHESION MOLECULE EXPRESSION IN PROSTATIC CARCINOMA

Ö. Cuhadaroglu, C.G. Sauer, R. Grobholz. *Pathologisches Institute, Universitätsklinikum Mannheim der Universität Heidelberg, Germany.*

Background: Neuroendocrine (NE) differentiated tumor cells can be recurrently found in prostatic carcinoma (PCa). NE tumor are involved in the proliferation of the surrounding tumor cells by paracrine mechanisms. The loss of E-cadherin and β-catenin is a central factor for local invasion and metastasis. To evaluate the relationship between NE tumor differentiation and the expression of E-cadherin and β-catenin was correlated with NE differentiation.

Methods: This study included 102 previously untreated PCa tissue specimens with a low (LNE) or high (HNE) NE differentiation. The intensity and cellular localization of E-cadherin and β-catenin was evaluated by immunohistochemistry. A homogeneous membranous staining in >70% of the tumor cells was regarded as normal, whereas an altered cellular distribution or heterogeneous staining in >30% of the tumor cells was regarded as aberrant. The expression of E-cadherin and β-catenin was correlated with the NE differentiation.

Results: Aberrant expression of E-cadherin and β-catenin was found in 72.7% and 90.2% of the tumors, respectively. In HNE tumors aberrant expression was significantly increased compared to LNE tumors ($p = 0.010$ for E-cadherin and $p = 0.016$ for β-catenin). In addition, NE cells of which 78.2% were located at the invasion front did not express E-cadherin or β-catenin as demonstrated by comparing serial sections.

Conclusions: Tumors with a HNE differentiation have a significantly decreased expression of the cell adhesion molecules E-cadherin and β-catenin which were absent in the NE tumor cells. These results indicate that NE tumor cells might influence the cell–cell adhesion by paracrine mechanisms and play an important role in tumor progression and invasiveness.

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P12. EXPRESSION OF MUC18 (CD146) IN HUMAN CHOROIDAL MELANOMAS

M.C. Madigan[a], V. Sharma[a], K. Lai[a], M.J. Jager[b], R.M. Conway[a]. [a]*Clinical Ophthalmology, Save Sight Institute, University of Sydney, Sydney, Australia;* [b]*Leiden Medical Center, Leiden University, Leiden, The Netherlands.*

Background: Choroidal melanoma is the primary eye cancer in adults, and displays some features in common with cutaneous melanoma. MUC18 is an important diagnostic marker of cutaneous melanoma, with increased expression in tumors associated with metastatic potential. However, MUC18 expression in primary choroidal melanoma and melanocytes remains to be fully investigated. We examined a series of choroidal melanoma cell lines, melanocytes, and primary choroidal melanomas, for a possible association between MUC18 expression and more aggressive forms of choroidal melanoma.

Methods: MUC18 expression (protein and mRNA) was assessed in choroidal and metastatic melanoma cell lines using immunoblotting and RT-PCR. Sections of whole eyes with mixed spindle/epithelioid choroidal melanomas ($n = 18$) were immunolabelled using a polyclonal antibody to the extracellular domain of MUC18 (R&D), and visualised using peroxidase and VectorRed.

Results: Immunoblotting of lysates from melanoma cells showed a positive band ~113 kDa, and MUC18 mRNA was detected in all cell lines. Moderate/strong cytoplasmic MUC18 immunolabelling was seen in 5/18 primary tumors (mixed spindle/epithelioid, <18 months detection to enucleation). MUC18 immunolabelling was seen on tumor vasculature, and in some cases, on networks/channels, characteristic of more aggressive tumors. Tumor extracellular matrix showed MUC18 immunolabelling in some cases.

Conclusions: Melanoma cell lines all expressed MUC18, however, only some primary choroidal melanomas, mostly with features suggesting more aggressive histopathology, expressed moderate/strong MUC18 immunolabelling. These observations suggest that MUC18 may play a role in tumor progression in some cases, and may be an appropriate marker for more aggressive choroidal melanomas.

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P13. RalA AND RalB PROTEINS CONTRIBUTE TO METASTASIS STIMULATION THROUGH DISTINCT PATHWAYS

V. Rybko, K. Ukraintsev, A. Martinjuk, N. Dyakova, A. Komelkov, O. Kovaleva, E. Tchevkina. *Oncogenes Regulation Laboratory, Institute of Carcinogenesis, Cancer Research Center, Moscow, Russia.*