Methods: Immunohistochemical analysis were performed on serial frozen sections using the $\alpha v\beta 3$-complex specific monoclonal antibody LM609.

Results: Variable levels of LM609 staining were found in all carcinoma lesions. A considerable number of tumor tissues (35/50) expressed $\alpha v\beta 3$ on more than 50% of their vessels. Inflammatory infiltrates and the possibly hypoxic conditions near necrotic areas of tumors were accompanied by an increased $\alpha v\beta 3$ expression. Remarkably, the vasculature in apparently normal tissue also stained for $\alpha v\beta 3$. However, the percentages of stained vessels and the staining intensity were lower than in neoplastic tissues. Besides the vascular $\alpha v\beta 3$ expression, several extravascular cell types stained positive, both in normal and tumor specimens.

Conclusion: Taken together, our findings show a considerable number of colon, pancreas, lung and breast carcinoma lesions with many $\alpha v\beta 3$-expressing vessels that could be targets for anti-$\alpha v\beta 3$ therapy.

209 POSTER

Liaison® free PSA, development of an automated chemiluminescence immunoassay for the determination of free prostate specific antigen (fPSA)

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Total PSA (tPSA) exists in human serum in two major detectable forms; PSA complexed to alpha1-antichymotrypsin (PSA-ACT) and free PSA (fPSA). Recent publications have shown that patients with benign prostate hyperplasia (BPH) tend to have higher levels of fPSA than patients with prostate cancer. The potential use of the ratio between the measured fPSA and tPSA concentration might be for the better differentiation of prostate cancer and benign disease. Liaison® fPSA is a rapid, fully automated immunoassay designed to run on the new random access Liaison® immunoassay analyzer from Byk-Sangtec Diagnostica. Liaison® fPSA is based on paramagnetic particles (Dynabeads®) for separation and a chemiluminescent label of isoluminol type with flash light kinetic. The assay is designed as a one-step two-site immunoluminometric assay using two highly specific monoclonal antibodies from Centocor (Centocor, Inc., Malvern) recognizing two different epitopes on the fPSA antigen. The monoclonal antibodies from Centocor bind only to free PSA when fPSA and ACT-PSA antigen material from Prof. Stamey, Stanford University (as reference) was used for evaluation. 100 μl sample are incubated together with 150 μl tracer antibody and the monoclonal antibody coated on the paramagnetic particle. After 10 min incubation time the paramagnetic particles are washed and unbound material is separated. Measurement of luminescence is performed for 3 s after injection of two trigger solutions. With the one-step 10 min incubation protocol, time to first result on the Liaison® analyzer is approx. 15 min. The Liaison® fPSA assay covers a clinical concentration range of 0–50 ng/ml with typical within-assay precision below 5% and sensitivity below 0.01 ng/ml respectively. The between-assay precision ranged from 4 to 8%. No hook effect is found up to 20,000 ng/ml. Samples run on the Liaison® fPSA assay show a good linearity upon dilution (±10% of the theoretical sample value). Method comparison (n = 72) of the Liaison® fPSA assay to an established method (Tandem-R Free PSA, Hybritech, Inc.) demonstrates a correlation coefficient of 0.96 and a slope of 0.96. In conclusion the Liaison® fPSA offers a rapid, reliable and precise method for the fully automated determination of fPSA.

210 POSTER

Expression of matrix metalloproteinase 7 (MMP-7) in alimentary tracts cancer, lung cancer and breast cancer

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Purpose: Proteolytic degradation of the extracellular matrix is an important part of tumor invasion and metastasis, and matrix metalloproteinases (MMPs) which are produced and secreted in tumor tissues have been implicated. MMP-7, also known as matrilysin, pump-1 is a member of stromelysin subclass of MMPs, and MMP-7 has wide range of substate specificity. However, stromelysin 1 (MMP-3) and stromelysin 3 (MMP-11) have been shown to express only in stromal cells in cancerous tissues. In this study, we have investigated whether MMP-7 expressed in cancerous tissues and/or tumor cells.

Methods: We have investigated the expression of MMP-7 colorectal, gastric, esophageal, lung breast cancerous tissues using reverse transcription polymerase chain reaction (RT-PCR), and the immunolocation of MMP-7.

Results: The incidence of MMP-7 mRNA expression were 60% in esophageal cancerous tissues, about 50% in gastric cancer and colorectal cancer, about 40% in lung and breast cancer, respectively. In contrast, MMP-7 mRNA expression was not detected in non-cancerous tissues excluding esophageal tissues associated with dysplasia. Immunolocalizational study demonstrated that MMP-7 was restricted in tumor cells

Conclusion: These results suggest that MMP-7 may be expressed in tumor manner and play a role in tumor progression.

211 POSTER

RENCA – An animal model for the development of anti-angiogenic strategies

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Purpose: RENCA, a murine renal cell carcinoma, metastasizes similarly to human cancer. VEGF (vascular endothelial growth factor) is the most important tumor derived angiogenic growth factor. We studied the importance of the VEGF-system for the RENCA- model and its use for screening of VEGF and VEGF receptor inhibitors.

Method: RENCA-cells were injected sc, iv or ir in syngenic Balb/c mice. VEGF-expression were measured by both, Northern-blot analysis and VEGF-Elisa. Primary tumors and metastases were analyzed for vessel density and VEGF-expression by immunohistology.

Results: Supernatants of cultered RENCA-cells were able to stimulate the proliferation of endothelial cells (HUVEC). This proliferation was dependent on the secretion of VEGF. Immunohistological staining of primary tumors and metastases showed elevated vessel density in correlation with VEGF-staining.

Conclusions: We showed that the RENCA model depends on the expression of VEGF and we will use this model to establish anti-VEGF-based therapies.

212 POSTER

Are serum TPS levels important in the prognosis of lung cancer?

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Purpose: The prognostic significance of tissue polypeptide specific antigen (TPS) were investigated together with other tumor markers such as NSE and CEA in SCLC and NSCLC patients. The serum levels of these markers were also compared with those of the patients with benign pulmonary disease (BPD).

Methods: Serum samples were obtained prior to treatment in 158 patients. The study group consisted of 72 SCLC, 44 NSCLC and 42 BPD cases and 23 healthy subjects. For TPS analysis, TPS-Elisa (BEKI) kit and the method of sandwich ELISA were used. In the analysis of NSE and CEA, NSE-RIA and CEA-RIA (CIS) kits and RIA were applied.

Results: All three tumor markers were significantly higher in lung cancer cases than in patients with BPD and healthy subjects. Serum TPS levels were highest in NSCLC. TPS and others were significantly higher in disseminated SCLC than limited disease. Also, in NSCLC cases, TPS and CEA were elevated significantly related with the stage groups. Evaluating the tumor markers with performance status (PS) and survival, TPS serum levels provided the better correlation with PS and survival in cancer cases than the other markers. Survival was significantly better in cases with TPS levels below 200 U/L, NSE levels below 20 ng/ml and CEA levels below 10 ng/ml in SCLC cases. When the same values were applied to NSCLC cases, TPS and CEA exhibited significant differences in survival.

Conclusion: The significant correlations between TPS with stage, PS, survival suggest that the use of this marker together with NSE and CEA in SCLC patients and together with CEA in NSCLC patients may contribute to the clinical evaluation.