expression status of Cyr61. Correlations of Cyr61 over-expression with various clinicopathologic factors were also determined. Statistical analysis was performed to explore the links between expression of the Cyr61 and clinicopathological parameters.
Results: On Western blot analysis Cyr61 up-regulation was observed in colorectal cancer tissues (17/21,80.9%). In 234 colorectal cancers, tumour tissue microarray revealed significantly up-regulated Cyr61 protein expression in colorectal cancer tissues versus normal tissues adjacent to tumour. Cyr61 expression was high in 136 of 234 cases of colorectal carcinomas (58.1%). Cyr61 over-expression was significantly associated with TNM stage ($P = 0.012$) and regional lymph node involvement ($P = 0.018$). Kaplan–Meier survival analysis showed that over-expression of Cyr61 was related to poor survival of colorectal cancer patients ($P = 0.031$). But significant associations were not found between Cyr61 expression versus tumour grade, age and gender.
Conclusions: Our results suggest that Cyr61 is highly expressed in colorectal carcinomas and Cyr61 may play a role in the progression of colorectal cancers. Also, Cyr61 might be a new molecular marker to predict the prognosis and serve as valuable targets for therapeutic intervention of patients with colorectal carcinoma.

1147 POSTER

Inter-reader Agreement in Response to Therapy Evaluation of Advanced Lung Cancer: Benefits of a Volume-derived Imaging Biomarker

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Background: Imaging-based endpoints are used to assess cancer response to therapy with lesion size-based criteria such as RECIST. Recent initiatives from interdisciplinary communities investigate other imaging biomarkers such as lesion volume. As discordance in the response evaluation is a critical issue, the expected benefit of a novel biomarker should be an improvement of the inter-reader agreement. The goal of this study is to evaluate the impacts of a volume-based measurement on the inter-reader variability.
Material and Methods: A retrospective study was performed on 10 patients having at least one Non-Small Cell Lung Cancer (NSCLC) lesion. These patients were followed over time with an average of 7 Computed Tomography (CT) studies. 3 readers delineated the volume of each lesion at each time point. Volume was automatically computed after a semi-automatic segmentation completed slice-by-slice with help of a manual tool. From the volume delineation, Longest Axial Diameter (LAD) and Spherical Equivalent Diameter (SED) were extracted. For each patient 2 response evaluations were performed according to RECIST thresholds based on LAD and SED. Quantitative inter-reader variability was analyzed relying on non-parametric statistics of Bland-Altman limit of agreement. Inter-reader agreement of the Best Overall Response was analyzed using Kappa coefficient.
Results: The variability in the measure was reduced from 26% (LAD) to 21% (SED). This benefit in measurement brought an improvement in the inter-reader agreement from Kappa = 0.15 (LAD) to 0.55 (SED).
Conclusions: We measured a reduction of quantitative variability using SED instead of LAD and an improvement of the inter-reader agreement.

1148 POSTER

DAB2 Interactive Protein (DAB2IP) Methylation in Serum DNA of Non-Small-Cell Lung Cancer (NSCLC) Patients (p) With Epidermal Growth Factor Receptor (EGFR) Mutations

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Background: DAB2IP loss promotes primary tumour growth by activating Ras and drives metastasis through NFkB, serving as a signaling scaffold to coordinately regulate these pathways. DAB2IP is frequently methylated in lung cancer, and methylation in the m2a region is a key regulatory factor for DAB2IP expression in prostate cancer. We examined DAB2IP methylation in cell lines and in serum from erlotinib-treated NSCLC p with EGFR mutations.
Material and Methods: In human lung, breast and colorectal cancer cell lines, we analyzed DAB2IP promoter methylation in regions m2a and m2b by methylation-specific PCR (MSP) and bisulfite genomic sequencing. In circulating serum DNA from 152 erlotinib-treated NSCLC p with EGFR mutations, we analyzed methylation in the m2a and m2b promoter regions of DAB2IP by MSP. Methylation status was correlated with clinical outcome.
Results: Methylation was detected in the m2a region of 42 (27.63%) p, and in the m2b region in 51 (33.55%) p. There were no major differences in clinical characteristics (age, gender, smoking history, EGFR mutation type, metastatic sites) between p with methylation in the m2a region and p with methylation in the m2b region. Overall progression-free survival (PFS) was 15 months (m), and median survival (MS) 28 m for all 152 p. For the 41 p with bone metastases (mets), PFS was 14 m for 30 p without methylation in the m2a region vs 8 m for 11 p with methylation in the m2a region (P = 0.01), and MS was 23 m vs 10 m, respectively (P = 0.19). For the 57 p with distant mets but no lung mets, PFS was 18 m for 36 p without methylation in the m2a region vs 10 m for 21 p with methylation in the m2a region (P = 0.01), and MS was 24 m vs 16 m, respectively (P = 0.03). No differences in either PFS or MS were observed according to the methylation status of the m2b region.
Conclusions: Methylation in the m2a region of DAB2IP in serum DNA correlates with PFS and MS to erlotinib in NSCLC p with EGFR mutations with non-lung mets. Surveillance of DAB2IP methylation status in circulating DNA could be a useful tool to predict outcome to erlotinib in EGFR-mutated NSCLC p with non-lung mets.

1149 POSTER

Patient-derived Tumourgrafts − Models for a Systemic Cancer Biology Research

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Background: Cancer is a complex genetic disease leading to a high variety of phenotypes among the different individuals. Each tumour presents a very specific pattern of molecular changes and responses to drugs. The correct identification of predictive biomarkers selecting the most appropriate therapies and avoiding unnecessary treatments for an individual patient is still a challenge. Patient-derived tumourgrafts allow preclinical investigations in a clinically relevant way. We performed investigations to improve the understanding of cancer complexity and to draw rational conclusions for therapy decisions.
Methods: The tumour models were established by direct transplantation of surgical specimens to immunodeficient mice and were maintained in early passages. A high congruence between original patient sample and xenograft could be proven both at gene and protein level. The following tumourgrafts are available: 10 breast, 28 colo-rectal, 25 lung, 6 ovarian, 10 sarcomas, 25 ALL, 5 AML. We will show examples for which purposes the models are appropriate and focus on non-small cell lung (NSCLC) and colon cancer.
Results: The xenografts were characterized for response towards clinically used cytotoxic and novel targeted drugs. The analysis for mutations revealed that all NSCLC models were *EGFRwt*, 5/25 were *KRASmut* and 12/25 were *P53mut*. None of the mutations correlated with response to therapy. In the colon cancer xenografts *KRAS, BRAF* and *PIK3CA* mutations predicted resistance to Cetuximab.
Using Affymetrix based gene profiling we identified a potential set of 20 genes which were differentially expressed between Oxaliplatin responder and non-responder.
In a preclinical Phase II study, the response of 22 NSCLC xenografts to a novel Epothilone was evaluated; *P53* mutations and overexpression of a cytochrome P450 enzyme were identified as potential biomarkers for the stratification of patients. The individual comparison of responses of colon cancer patients and their derived xenografts resulted in a congruence in 5 out of 5 patients included.
Conclusions: Patient-derived xenografts are a valuable model system to address clinically relevant questions in a standardized and strictly controlled fashion. They show a high concordance with the clinical specimens concerning marker expression and response to therapy.

1150 POSTER

Analysis of Biological Markers, Tumoral Predictors and Clinical Features as Prognosis Factors to Cnemotherapy Response in Metastatic Carcinomas of Unknown Primary Site

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Background: The authors investigated prognosis factors to chemotherapy response such as clinicopathological features: age, gender, performance