Conclusions: Our recently presented biomarker-platform derived from a Pten conditional knockout mouse model showed high feasiblity for the identification of predictive markers for therapy response to docetaxel chemotherpay in human patients with mCRPC. The analysis of the biomarker signature combining two of these candidate biomarkers therefore warrants further investigation in a bigger collective of patients.

1431 POSTER

Application of Native Fluorescence of Blood Plasma in Colorectal Cancer Detection: Results of a Prospective Study

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Background: Fluorescence spectroscopy of biomolecules is considered a promising method to *in vivo* discriminate normal tissue from malignant tissue in various sites, including breast, cervix, lung, and colon. In the present work we investigated the possible role of the native fluorescence of blood plasma in discriminating patients with colorectal cancer from subjects of a control population. Approval for this research was obtained from the Ethics Committee of our Institute; the study was registered in ClinicalTrials.gov with the code NCT01286064.
Methods: In this preliminary phase, the study involved 100 subjects: 50 healthy subjects with negative result from colonoscopy (40% male and 60% female; mean age 58.0) and 50 patients bearing colorectal adenocarcinoma (44% male and 56% female; mean age 60.2). All participants gave written informed consent and completed questionnaires on their diet, lifestyle and medical history. Blood samples were collected from all the subjects and plasma fluorescence spectrum was analyzed using a conventional spectrofluorimeter.
Results: The intensity of the fluorescence emission peak around 615–635 nm of the collected blood samples was significantly different between patients bearing colorectal cancer (median value 14.94 a.u., mean 16.01±4.87 a.u.) and healthy subjects (median value 13.35 a.u., mean 14.06±3.79a.u.), with the minimum p level at 623 nm ($p < 0.0001$). Data on height and weight, alcohol use, red meat and vegetables intake, smoking status, concomitant illness and familial tumour history were used with the fluorescence intensity at 623 nm for setting up a neural network classifier designed to perform automated diagnosis. Not all the variables were included in the network input, because some of them did not add any significant improvement to the discrimination. Variables retained as input data over intensity of fluorescence were body mass index, sex and familial tumour history. The neural network capability in discriminate healthy subjects from patients bearing colorectal cancer was tested by ROC analysis, which resulted in an AUC of 0.81.
Conclusion: According to our results, a possible application of the fluorescence measurements of blood plasma in colorectal cancer detection would seem justified. Work is in progress to asses the true clinical value of the test on a larger number of subjects.

1432 POSTER

Pharmacogenetic Assessment of Toxicity After Docetaxel Chemotherapy in Breast Cancer

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Background: Taxanes are the most active agents in the treatment of breast cancer. However, the utility of taxane-based therapy is limited principally by gastrointestinal and hematological toxicity, hypersensitivity and cumulative neurotoxicity. To understand why only some patients experience severe adverse effects the metabolic pathways of this drug have to be unraveled in detail. Docetaxel is metabolized by CYP3A4 and CYP3A5 and is a substrate for the ATP binding cassette multidrug transporters ABCB1. The aim of our study was to evaluate the association between docetaxel-toxicity and genetic polymorphisms related to its metabolism through peripheral venous blood sampling in patients with breast cancer undergoing chemotherapy.
Materials and Methods: We studied 100 patients (age 53.3±8.5DS) affected by breast cancer under treatment with docetaxel as adjuvant or metastatic therapy; we genotyped them for selected polymorphisms and ABC-transporters that may influence cellular sensitivity to taxanes: CYP3A4* 1B (A > G), CYP3A5* 3 (G > A) and ABCB1 (1236 C > T; 3435 C > T). SNPs (single nucleotide polymorphisms) were carachterized by pyrosequencing. The statistical survey was conducted by SPSS 14.2 software.
Results: We observed a significant association between patients homozygous for ABCB1 polymorphisms and a lower toxicity after therapy with docetaxel. For CYP3A4* 1B and CYP3A5* 3, although without statistical significance ($p > 0.005$) we can dimostrate a greatest exposure to the toxicity of docetaxel, presumably due to increased production of reactive metabolites.
Conclusions: We suggest that CYP3A4, CYP3A5 and ABCB1 might affect taxane toxicity therefore representing, if confirmed in a larger cohort of patients, a toxicity predictive biomarker. In the future, studies with SNP chips and other studies on the transcriptome, proteome and metabolome level should be performed in order to identify signatures differentiating between patients with high or lower toxicity linked to docetaxel chemotherapy.

1433 POSTER

Diagnostic Ability of TPSa and CPSa in a Patient Cohort Referred to a Danish Urological Department

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Introduction: Both total-PSA (tPSA) and complexed-PSA (cPSA) have been advocated for diagnosis of prostate cancer (PCA). However it remains unclear which of these two PSA forms has the best diagnostic efficiency.
Materials and Methods: 1423 consecutive patients referred to the Department of Urology from general practitioners during June 2005 to August 2006 were included in the study. 161 patients with previously known Prostate Cancer (PCA) were excluded, leaving 1262 patients for diagnostic procedures. Of these, 299 patients were diagnosed with PCA and 963 patients were found without PCA at the time of inclusion. Blood samples were collected in tubes with gel separation, centrifugated and the serum frozen within 1 hour for later analysis tPSA and cPSA were measured by the Bayer/Siemens chemiluminescent assays on an ADVIA Centaur automated analyzer.
Results: tPSA and cPSA levels among the 299 PCA patients ranged from 0.06–5920.50 μg/l and 0.06–4908.70 μg/l, respectively with medians of 13.39 μg/l and 10.86 μg/l. tPSA and cPSA levels in 963 patients without PCA at the time of investigation ranged from 0.06–233.49 μg/l and 0.06–83.82 μg/l, respectively with medians of 2.81 μg/l and 2.10 μg/l. The sensitivity of tPSA and cPSA were 97.7% and 97.3%, respectively ($p > 0.05$). The specificity of tPSA and cPSA were 60.4% and 65.1%, respectively ($p > 0.05$). PVpos of tPSA and cPSA were 39.3% and 42.2%, respectively ($p > 0.05$). PVneg of tPSA and cPSA were 99.0% and 98.9% respectively ($p > 0.05$). Efficiency of tPSA and cPSA were 68.1% and 71.8%, respectively ($p > 0.05$).
Conclusion: The diagnostic ability of tPSA and cPSA is similar ($p > 0.05$). The tPSA and cPSA concentrations among patients referred to the Department of Urology from general practice were surprisingly high indicating late referral.

1434 POSTER

Impact of KRAS Mutations (Krasmut) on Clinical Outcome in Stage IV Non-small Cell Lung Cancer (NSCLC) Patients (pts) and Their Relationship With Other Biomarkers

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Background: Kras accounts for 90% of RAS mutations in lung adenocarcinoma and approximately 97% of Krasmut in NSCLC involve codons 12 or 13. Kras tumour status cannot be easily predicted on the basis of smoking history alone. Krasmut status might help in the prediction of clinical outcome for pts receiving different treatments. The role of Krasmut as a predictor of response for pts with stage IV NSCLC treated with chemotherapy alone is poorly understood. Emerging data suggest that Krasmut are negative predictors of benefit from both adjuvant chemotherapy and anti-EGFR-directed therapies.
Material and Methods: From August 2009 to January 2011 we analyzed Krasmut in samples from 114 stage IV NSCLC pts. We analyzed different types of Kras point mutations in codons 12 and 13 by direct DNA sequencing from paraffin-embedded tumour tissue (PETT). We also used DNA sequencing from PETT to analyze other mutations (EGFR) and mRNA gene expression to evaluate BRCA1and RAP80 levels. We evaluated the presence of Krasmut according to histological subtype.
Results: Krasmut were found in 21.9% (25 /114). Out of pts harboring Krasmut the median age was 59 y, 64% were male. According to smoking status 8% were never smokers, 32% former smokers and 60% current smokers. According to histology 72% were adenocarcinoma, 12% squamous cell carcinoma and 8% bronchioloalveolar carcinoma. According to PS ECOG 44% were PS0, 32% PS1 and 24% PS2. The distribution of