of *MPL* mRNA in NCI-H510 cells did not correlate with detectable TpoR protein expression. Erythropoietin receptor (*EPOR*) mRNA was expressed at low-to-moderate levels, while *ERBB2* and *IGF1R* were expressed at higher levels. Microarray analysis showed undetectable *MPL* mRNA levels in all breast cancer and RCC samples and low levels in 48% NSCLC samples. In contrast, *EPOR* was expressed in 75–100% of the breast cancer, NSCLC, and RCC samples. *ERBB2* was expressed in 81–100% of the samples and *IGF1R* was expressed in 54–100% of the samples. For breast tumors, the levels of mRNA expression were as follows: *MPL* < *EPOR* < *IGF1R* < *ERBB2* < *epor* < *igf1r* < *erbb2* </>. By qRT-PCR, there were also low or undetectable levels of *MPL* expression in these samples from subjects with prostate, ovarian, lung, and breast tumors. *EPOR*, *ERBB2*, and *IGF1R* expression vary according to tumor type, but were generally higher than *MPL*.
Conclusions: In summary, low or undetectable levels of *MPL* mRNA expression were observed in most tumor cell lines and in most samples of patient tumors, compared with *EPOR*, *ERBB2*, and *IGF1R*.

1094 POSTER

Influence of TGFB1+869T>c polymorphism in non-small cell lung cancer (NSCLC) risk

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Background: Lung cancer (LC) is the third most common type of cancer in Europe and was the first cause of death by cancer in 2006. Non-small cell lung cancer (NSCLC) accounts for 75%–85% of all histological types of lung cancer. Lung carcinogenesis is complex and a multi-step process, resulting from exposure to environmental and genetic factors. The transforming growth factor beta 1 (TGFβ1) is a multifunctional regulatory polypeptide that controls many aspects of cellular function (cellular proliferation, differentiation, migration, apoptosis, immune surveillance). Nevertheless, TGFβ1 has been suggested to play a dual role, acting as a suppressor in early stages and as a tumor promoter in later stages. *TGFB1+869T>C*, is a functional polymorphism described in *TGFB1* gene responsible for a T-to-C substitution at nucleotide 29 of codon 10. This transition has been associated with higher circulating levels of TGFβ1, that may influence LC development and prognosis. Our purpose was to investigate the role of *TGFB1+869T>C* functional polymorphism in NSCLC risk.
Material and Methods: DNA was extracted from peripheral blood cells of 1099 individuals: 305 patients histopathologically diagnosed with NSCLC and 794 healthy individuals without evidence of neoplastic disease. Genotyping of *TGFB1+869T>C* polymorphism was performed by Real-Time PCR allelic discrimination method. The odds ratio (OR) and its 95% confidence interval (CI) were calculated as a measure of the association between *TGFB1+869T>C* genotypes and NSCLC risk.
Results: The frequency of the TT genotype was lower in LC patients than in controls (29% and 37%, respectively). Conversely, we found an overrepresentation of C carriers in NSCLC group in comparison with normal controls (71% and 63%, respectively). Carriers of the C allele had an increased risk for NSCLC development (OR = 1.44, 95%CI = 1.07−1.94, $P = 0.012$). Stratification according to histological type, showed a statistical significant increased risk for epidermoid NSCLC development in the individuals with C carrier genotypes when compared to individuals with TT genotype (OR = 1.68, 95%CI = 1.05−2.72, $P = 0.023$).
Conclusions: Individual differences in cellular microenvironment may influence the susceptibility to cancer development and behaviour. Our results suggest that *TGFB1+869T>C* functional genetic polymorphism influence NSCLC susceptibility. This genetic profiling may help define higher risk groups for an individualized therapy.

1095 POSTER

Pharmacogenomic analysis of the triplet combination of gemcitabine, oxaliplatin and cetuximab as salvage therapy for metastatic colorectal cancer (mCRC) patients

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Background: We have previouslyreported that the combination of biweekly gemcitabine-based therapy wasactive in pretreated mCRC pts (De la Cruz et al, ASCO GI 2008, abstr377). We aimed to investigate whether germ line polymorphisms may bepredictors of clinical outcome in mCRC pts treated with thiscombination.
Material and Methods: We evaluated SNPs ofgenes involved in gemcitabine metabolism (CDA, dCDK, RRM1, DCTD, SLC28A1), DNA repair (XRCC1, XRCC 3, ERCC1, XPD) and two IgG Fragment CReceptor polymorphisms (FcgRIIa- H131R and FcgRIIIa-V158F) reported tobe predictive of cetuximab-based therapy, even in K-ras mutatedpts. Whole blood was collected and DNA extracted from peripherallymphocytes using a DNA isolation Kit (Qiagen, CA). Polymorphisms weredetected using the TaqMan genotyping assays (Applied Biosystems, CA). Clinical response was evaluated according to RECIST criteria. Univariate analysis (Fisher's exact test for response; log-rank testfor TTP and OS) was performed to examine associations betweenpolymorphisms and clinical outcome.
Results: Blood samplesof 35 out of 39 enrolled pts were tested for genomic analysis. Patient's characteristics are as follows; M/F: 26/13, median age: 59 years, median number of prior chemotherapy lines: 2 (1−4), Köhne riskgroups; low: 8 pts, intermediate: 18 pts, high: 13 pts. After a medianfollow-up of 20 months, median progression-free survival (PFS) is 6.7months (95% CI; 5.2−8.3) and median overall survival 15.4 m (95% CI;14.7−16.1). Overall response rate (ORR) was 53.8%. RRM1 R284R ($p = 0.06$),T741T ($p = 0.02$) and RRM1–524CT ($p = 0.04$) were linked to clinicalresponsiveness. All pts possessing 2 or 3 favourable RRM1 SNPsresponded. ORR was 53.3% for pts with no favourable SNPs versus 85% forthose pts with any favourable SNP ($p = 0.04$). ORR was also significantlyhigher in pts with any histidine allele in the FcgRIIa polymorphism (93% vs. 60%, $p = 0.034$).
Median PFS was adversely affected in ptsharbouring no favourable RRM1 SNPs (4.2m versus 6.7 months, $p = 0.019$) and in those pts with homozygous FcgRIIa-131R allele (4.4 vs. 7.5months, $p = 0.007$).
Conclusions: Polymorphic variants of RRM1 and FcgRIIa may play a key role in the efficacy of gemcitabine-based therapy for mCRC pts.

1096 POSTER

Molecular signatures of disseminated tumour cells in metastatic breast cancer patients

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Background: The critical step in breast cancer progression is the spreading of tumor cells to distant organs. Numerous studies have demonstrated that the presence of Disseminated Tumor Cells (DTC) in the bone marrow from patients with breast cancer is an independent prognostic factor for systemic relapse and breast cancer related death. Immunocytochemical methods for detection of DTC make it possible to identify single DTC in a population of normal cells. However, we still have limited knowledge about the biological and molecular characteristics of the DTC themselves. Complete genomic profiles and expression patterns have to be considered in order to understand tumor aggressiveness, clinical outcome and/or the disseminated tumor cell status.
Material and Methods: Mononuclear cells from the bone marrow of metastatic breast cancer patients are transferred to slides, DTC are identified by immunocytochemical staining and isolated by micromanipulation. Samples are amplified by single cell whole genome amplification and the resulting amplified DNA is applied to high density whole genome Agilent CGH arrays.
Results: We tested and established the Single Cell array Comparative Genomic Hybridization (SCaCGH) technique in our laboratories in order to investigate the molecular signatures of DTC in metastatic breast cancer patients. DTC from the bone marrow of metastatic breast cancer with variable numbers of DTC per mononuclear cells were selected and analyzed. In a first pilot of about 10 patients we compare the genomic profiles of 1−3 DTC per patient in relation to each other and among different patients. Our preliminary results show concordance of the genetic profiles from different DTC within a patient and different copy number variations among the DTC from different patients.
Conclusions: Due to the implementation of a technique called the Single Cell array Comparative Genomic Hybridization (SCaCGH) we are finally able to characterize single cells using high density microarrays. This will provide us with information about the properties of DTC important for the understanding of the metastatic cascade, apart from the potential to better understand tumor heterogeneity in general.