epidermal subcellular fractions were isolated. JNK activity was assessed after immunoprecipitation and incubation with substrate peptides. Phosphorylated peptides were detected using phosphoserine-specific antibody. AP-1 and STAT activation was evaluated using the commercially available ELISA kits (Transcription Factor TransAM Kits from Active Motif, USA).
Pretreatment with the tested phenols decreased TPA stimulated JNK and AP-1 activation, with TAA being the most potent and PCA the weakest compound. TAA did not affect STAT3 and STAT5B activation, whilst PCA was found to be their most potent inhibitor.
The results indicate that modulation of JNK by plant phenolic acids may be considered as a possible mechanism of their chemopreventive activity. Moreover, possible functional cross-talk between JNK and AP-1 or STAT activation is postulated.

776 An eleven-gene signature of normal and cancerous lung tissues

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Current paradigms suggest lung cancers are caused by gene transcriptional activation/or progression events. Gene expression profiling has been used as molecular diagnostic tool for classification and staging of cancers. It can be also effectively used to determine the molecular targets for personalized treatment. We have used a panel of 11 genes expression signature to characterize surgically removed human lung cancers specimens as well as patient's noncancerous lung tissues. The panel includes 6 well studied oncogenes such as bcl-2, c-myc, ki-ras, c-ha-ras, her-2/neu and Tgf-α that represent excellent therapeutic targets. Other genes are, p53 (best known tumour suppressor), MDM2 (known for regulating p53), Mmp1 and Mmp14 (metastatic genes) and MDR1 (a well known drug resistant gene). We have evaluated over 50 pairs of noncancerous lung tissue and corresponding primary lung tumour tissues from lung cancer patients who had undergone surgical resection from 2008 to 2009. All tissues were collected fresh, snap-frozen and stored at −80ºC. Total RNA was isolated from all tissues with RNeasy mini kit (Qiagen) according to manufacturer's instructions. The cDNAs were then used for qRT-PCR analysis using, Step OnePlus™ (ABI). The expression profile of 11 genes was quantified with the use of Power SYBR Green PCR master Mix (ABI). Human b-actin was used as an endogenous control. Relative quantitation of gene expression was determined, using comparative CT method of (DDCT). Roughly over 70% of lung cancer patients show elevation in the expression of at least one apoptotic target genes (ki-ras, bcl2 and c-myc) with k-ras being overexpressed in about 50% of our patients. In conclusion specific inhibitors of k-ras, c-myc and bcl-2 could provide more effective tools to combat lung cancer with little or no side effect.

777 Analysis of polymorphisms related to mir-608 in patients with chronic myeloid leukemia

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The purpose of this study was to investigate miRNA-608 role in response to therapy with tyrosine kinase inhibitors (Imatinib). In this study, we analyzed rs9762 SNP located in a miRNA-608 binding site of 3′UTR of BCR-ABL1 gene and rs4919510 SNP in the mature sequence of miR-608 in CML patients with different response to tyrosine kinase inhibitor therapy (Imatinib). These polymorphisms disrupt the negative effect of mir-608 on its target BCR-ABL1.
In our study 76 CML patients at the age of 15−65 were involved. Genomic DNA was extracted from peripheral blood leukocytes by standard phenol-chloroform method. Genotyping was performed by the PCR-RFLP technique.
Combination of genotypes affecting mir-608/BCR-ABL1 interaction (*GG in mir-608 binding site and/or *GG in mature miRNA itself) was revealed with 81% in CML patients with uneffective therapy. We suggest that mir-608 could possess oncosuppressing activity as mir-203 but it should be confirmed by further experiments.
miRNAs could be a perspective tool for therapy and polymorphisms affecting its regulation should also be considered.

778 Association of the homozygous wild genotype of the GSTP1 Ile105Val polymorphism with Hodgkin's lymphoma susceptibility and progression in Ukrainian individuals

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Background: Glutathione S-transferase P1 (GSTP1) is a member of the GSTenzyme superfamily that is important for the detoxification of several cytotoxic drugs and their byproducts. The gene coding GSTP1 is polymorphic. The polymorphism of the GSTP1 gene causes the substitution of isoleucine to valine at amino acid codon 105 (Ile105Val). The proteins encoded by the different alleles show different abilities to metabolize carcinogens and anticancer agents. In temporary time the data about the relationship of GSTP1 Ile105Val polymorphism with Hodgkin's lymphoma (HL) susceptibility and progression are still in discussion, the author's publications presented the contradictory data.
Material and Methods: The association of GSTP1 Ile105Val polymorphism with HL susceptibility and progression was analyzed. The case group was comprised of 56 patients with HL at diagnosis (median age: 31 years, range: 17−48; males: 26, females: 30, stages IA−IIA: 20, stages IIB + III−IV: 36) and 158 blood donors (median age: 38 years, range: 17−59; males: 69, females: 89). The HL was diagnosed according to the World Health Organisation (WHO) classification and staging by Ann Arbor. Genomic DNA from peripheral blood of all individuals was analysed for identification of genotypes of the GSTP1 using TaqMan Polymerase Chain Reaction (PCR) allelic discrimination assays.
Results: From the data of PCR analysis, all the patients and controls were divided into three genotypes of the GSTP1 gene: Ile/Ile, Ile/Val and Val/Val. The distribution of the genotypes of the GSTP1 gene in both control and patients did not differ significantly from those predicted by the Hardy–Weinberg distribution. Additionally, it was no differences in the frequencies of the Ile and Val alleles between patients and control group. Obtained results showed that the Ile105Val polymorphism of the GSTP1 gene is not association with HL susceptibility in our cases. GSTP1 genotypes were monitored in patients stratified by age, gender and stage of disease. We did not observe associations between demographic characteristics of the patients (age and sex) and GSTP1 genotype. The frequency of the homozygous wild genotype of the GSTP1 was higher in patients with advanced tumours (stages III−IV) and stage IIB than in patients with tumours of stages IA−IIA (47.2% versus 35%, $p < 0.02$). These results possibly could be an evidence of correlation between the homozygous wild allele of the GSTP1 gene and high aggressiveness of the HL in our cases, but it should be confirmed by further studies with larger cohorts of patients.
Conclusions: The received data suggest that the Ile105Val polymorphism of the GSTP1 gene is not directly involved in the development of HL, but homozygous wild genotype of this gene is linked with high aggressiveness of the HL in Ukrainian individuals.

779 Expression of TIMP-1 correlates with expression of pSTAT3 in breast cancer tissue

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Background: Constitutive activation of signal transducer and activator of transcription 3 (STAT3) has been found in a wide spectrum of human malignancies, such as prostate, breast and lung cancer. It has been shown that constitutive activation of STAT3 is important in the pathogenesis of breast cancer with a dual role, as an antiapoptotic molecule during tumour initiation as well as a critical regulatory switch governing cell cycle progression associated with tumour promotion. Tissue inhibitor of matrixmetalloproteinases (TIMP1) has also been shown to possess anti-apoptotic properties in some cancer cell types, including breast cancer. It has been shown in lymphoma that the expression of TIMP1 correlates with the STAT3 activation status. With this background, we hypothesize that STAT3 activation may modulate invasiveness of breast cancer by engaging TIMP1.
Material and Methods: We analyzed the expression of STAT3 and TIMP1 in breast cancer and in surrounding tissue of 30 patients (clinical stage I and II) in tumour cell lysates by Western blotting using anti-TIMP-1 and anti-STAT3 antibodies.
Results: TIMP1 expression in surrounding tissue significantly correlates with TIMP1 expression in tumour tissue of breast cancer patients ($p < 0.01$). We show that STAT3 expression in breast cancer tissue is significantly higher ($p < 0.01$) compared to its expression in the surrounding tissue. Moreover, we show that expression of pSTAT3 in cancer tissue significantly correlates with TIMP1 expression in this tissue ($p = 0.001$, $r = 0.76$).However, in the group of patients with smaller tumour size ($t < 10$ mm) expression of pSTAT3 in breast cancer tissue does not correlate with TIMP1 expression in the tumour ($p = 0.13$, $r^2 = 0.64$). In the group of patients with larger tumour size ($t > 20$ mm) the expression of pSTAT3 in breast cancer tissue correlates with TIMP1 expression in this tissue ($p = 0.048$, $r = 0.78$). Moreover, we found that tumour size in mm^3 correlate with expression of pTIMP1 in breast cancer ($p = 0.02$).
Conclusion: In this study we show that correlation of pSTAT3 and TIMP1 in breast cancer tissue is associated with larger tumour size, suggesting a role of these two parameters in tumour growth. As STAT3 activation participates in the mechanisms associated with cancer progression there is a need for consideration of STAT3 as possible targets in designing new therapeutics in breast cancer.