calculated as a measure of the association between CYP3A5*3 genotypes and NSCLC progression.
Results: The frequency of the GG genotype was 79.3% in LC patients and 86% in controls. The frequency of the heterozygous genotype A/G was of 20.3% in patients and 13.3% in controls. Homozygous individuals for the A allele where rare: 0.1% in LC patients and 0.6% in controls. The analysis of the genotypic frequencies of the CYP3A5*3 polymorphism indicates that individuals with GG genotype present a 38% protection for the development NSCLC (P = 0.020; OR = 0.621; 95% CI = 0.415−0.931).
Conclusions: Individual differences in the metabolism of carcinogens may influence the susceptibility to cancer development and behaviour. Our results suggest that that individuals with GG genotype present a lower risk of developing NSCLC than individuals with genotypes carrying the A allele (OR = 0.621). This is probably due to a decreased activation of procarcinogens present in tobacco smoke in result of the lack of CYP3A5 in individuals with genotypes carrying the CYP3A5*3 allele.

6537 POSTER

Selenite mediated cytotoxcicity in human lung cancer and the role of Thioredoxin reductase 1

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Background: The human selenoenzyme thioredoxin reductase 1 (TrxR1) is a very important enzyme for cell growth, differentiation, and the defense against oxidative stress. Several studies have shown that TrxR1 is upregulated in tumor cells and it is a target for many anti-cancer drugs. The regulation of TrxR1 is very complex and involves the expression of different transcript forms of mRNA.
Materials and Methods: We have, by quantitative polymerase chain reaction, investigated the total expression of TrxR1 mRNA and quantified the expression of alternative mRNA forms in five different human lung cancer cell lines. IC50 values for selenite were determined for the different cell lines and compared to the sensitivity towards doxorubicin.
Results: The results indicated an inverse relationship between resistance towards doxorubicin and selenite induced cytotoxicity. In addition, inhibition of TrxR resulted in enhanced selenite cytotoxicity. Selenium treatment resulted in increased expression of almost all TrxR1 mRNA variants while the TrxR protein activity decreased. Total TrxR1 and the less abundant forms were detected in human tissue samples from both squamous and adenocarcinoma from lung, using specific peptide antibodies. Expression of TrxR1_v.2, 3, 5 isoforms and Trx1 in the tumor correlated with degree of differentiation.
Conclusions: Our results show that TrxR1 is involved in selenite mediated cytotoxicity and investigation of alternative transcript variants of TrxR1 could further be a valuable tool in the diagnostics and characterization of tumors.

6538 POSTER

Preclinical studies on the antitumor activity induced by novel modified steroidal alkylating esters of propenoic acid against murine Lewis lung carcinoma (LLC)

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Background: The sensitivity of some neoplasms to hormonal intervention provides a rational basis for utilizing steroid hormones as a biological “platform” for cytotoxic agents in cancer therapy. The purpose of this study is to investigate the relationship between structure activity and antineoplastic effect of in vivo biological system, treated by five newly synthesized modified steroidal derivatives of p-bis(2-chloroethyl)aminophenylpropenoic acid (PK 11–PK 15).
Materials and Methods: The acute toxicity of the compounds was determined fol-lowing a single i.p. injection into C57BL mice in groups of 10 mice/dose. C57BL mice were used for the evaluation of the antitumor activity. Experiments were initiated by implanting the LLC cells. These were injected subcutaneously [0.2 ml tumor brei of 13 (w:v)]. Each treated group consisted of 6 mice and 8 mice comprised the control group, treated with saline only.
Results: The antitumor activity was assessed from the inhibition of tumor size (I) and from the oncostatic parameter (T/C).
Conclusions: The antitumor activity of compound PK 11 is distinctly superior to that of compounds PK 12, PK 14, PK 15, whose activity is marginal. Compound PK 13 is less effective than PK 11. Most likely, the highest effect of compound PK 11 is due to the presence of double bond in the homoazasteroidal nucleus (ring B) and the 3β-(cis) configuration.

Acute toxicity and antitumor activity of PK 11–PK 15 on LLC.

Compound	LD10 (mg/kg)	LD10 dose (mg/kg)	Treatment schedule	Growth inhibition (%)	T/C (%)
Control	–	Saline	–	0	100
PK 11	500	500	Day 1	57	194
PK 12	400	400	Day 1	28	127
PK 13	600	600	Day 1	42	171
PK 14	200	200	Day 1	21	124
PK 15	100	100	Day 1	19	117

6539 POSTER

Malignant mesothelioma of pleura: potentialities of immunocytochemistry

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Considering that surgical treatment is extremely traumatic, pathologist must be sure in the diagnosis. It is very important to use supplementary methods of diagnostics.
An objective of this work was to study potentialities of cytological diagnostics of pleural mesothelioma using immunocytochemistry. The data of 90 patients with malignant mesothelioma of pleura was investigated in Altai Oncological Hospital during 5 years including females 48 (53.3%) and males 42 (46.7%). Immunocytochemistry was used from 65 (72.2%) patients. Specimens were prepared using Centrifuge and Streptavidin-biotin system with a set of markers (11 antibodies).
Epithelioid mesothelioma was diagnosed in 82 cases (91.1%). The sarcomatoid variant of pleural mesothelioma was determined in 2 (2.2%) and biphasic in 6 (6.7%) cases. Both cases of sarcomatoid mesothelioma resemble fibrosarcoma. For differential diagnostics immunocytochemistry was used. The reactions with Cytokeratins (C MNF 116, C AE1/AE3) were most important. Biphasic mesothelioma contains both epithelial and sarcomatoid cells.
The cells of mesothelioma were positive with Keratins (C MNF 116, C AE1/AE3), also positive cytoplasmatic reactions with Vimentin were noticed in all cases of mesothelioma. The cells of tumours were immunonegative with mono- and polyclonal Carcinoembrionin antigen (CEA). Tumour cells had weak reactivity with polyclonal Carcinoembrionin antigen in 3.1% of cases. Immunonegative reaction of mesothelioma cells was noticed with Epithelial antigen (Ber-EP4).
All cases of mesothelioma (100%) showed positive reactions with Methotelial Cell (HBME-1). Calretinin and Thrombomodulin were studied only in 12 cases of mesothelioma (18.5%). Cells of mesothelioma with Calretinin had nuclear and cytoplasmaticstaining.It wasn’t noticed in cells of carcinoma excluding serous papillary of ovarian carcinoma. Metastases of carcinoma had immunonegative reactions with Thrombomodulin. Cells of mesothelioma showed negative reactions with CD-15. Immunoreactivity of Epithelial Membrane Antigen (EMA) was noticed in the membranes of cells.
The data show that the cells obtained for cytological examination have the same characteristics as those in biopsy materials. Sarcomatoid mesothelioma may be limited of Cytokeratins. Reactions with Calretinin, Mesothelin and Thrombomodulin are the most important for Epithelial Mesothelioma with positive reactions with Vimentin, Keratins. Immunonegative reactions with CEA, Ber-EP4 and CD-15 are typical.

6540 POSTER

p53 gene mutation, mrna expression, aberrant protein expression and clinicopathological features in resected non-small cell lung cancer

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Background: Functional abnormality of p53 plays a pivotal role in occurrence of malignant tumors including lung cancer. Aberrant expression of the p53 protein using immunohistochemistry has been investigated in many cancers. However, immunohistochemical detection cannot distinguish expression of wild type p53 protein from mutant one, so that clinical significance of p53 aberrant expression should be analyzed with regard to the presence or absence of p53 gene mutations. In this study, we investigated relationships among gene mutation, mRNA expression and aberrant protein expression of the p53, and analyzed their clinical