using fluorescence and CD spectroscopy. Anti-proliferative potential was determined using sulphorhodamine-B assays.
Results: *Arisaema utile* lectin (AUL) gave a single band in SDS-PAGE at pH 8.3 corresponding to subunit Mr 13.5 kDa. The native molecular mass of 54 kDa suggested a homotetrameric structure. Like other monocot lectins, AUL gave multiple bands in isoelectric focusing and in native PAGE at pH 8.3. AUL was inhibited by N-acetyl-D-lactosamine (LacNAc), a disaccharide and asialofetuin, a complex desialylated serum glycoprotein. When treated with denaturing agents, the lectin was stable in the presence of urea (3 M), thiourea (4 M) and guanidine HCl (4 M). The lectin had no requirement for divalent metal ions i.e. Ca^{2+} and $Mn^{2+}$for its activity. AUL was a glycoprotein with a carbohydrate content of 1.2%. Amino acid modification studies of AUL revealed the involvement of tryptophan and tyrosine residues involved in lectin-sugar interaction. AUL exhibited a fluorescence emission maximum (λ_{max}) at 340 nm upon excitation at 295 nm. Using Far UV CD spectra the estimated secondary structure was 37% α-helix, 25% β-sheet and 38% random contributions. *In vitro* anti-proliferative activity of AUL was tested on eleven different human cancer cell lines viz. MCF-7 (Breast), SK-N-SH (CNS), 502713 (Colon), Colo-205 (Colon), HCT-15 (Colon), HT-29 (Colon), SW-620 (Colon), Hep-2 (Liver), IMR-32 (Neuroblastoma), DU-145 (Prostate) and PC-3 (Prostate). The concentrations of AUL which produced 50% inhibition (IC_{50}) of cancer cell lines viz. SW-620, HCT-15, SK-N-SH, IMR-32, Colo-205 and HT-29 at 38, 42, 43, 49, 50 and 89 μg/ml. respectively.
Conclusion: The purified *Arisaema utile* lectin was found to be a homotetrameric protein with potent anti-proliferative effect on human cancer cell lines.

1073 POSTER

The relation between the change of functional cardiac parameters and single nucleotide polymorphisms in Glutathione S transferase P1 and Carbonyl reductase3 genes after doxorubicin chemotherapy

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Background: Glutathione S transferase P1 (GSTP1) is responsible for the detoxification of doxorubicin (Dox), and carbonyl reductase 3 (CRB3) converts Dox to doxorubicinole. Genetic variants of GSTP1 and CRB3 may be contributory to pharmacokinetic and pharmacodynamic variability of Dox, as well as to the interindividual differences in the toxic side-effects. Aim of this study was to investigate the relationship between genetic polymorphisms of GSRP1 (A313G) and CBR3 (V244M) and cardiotoxic effect of Dox assessed by ECG-gated blood pool SPECT (SPECT) and echocardiography (E).
Materials and Methods: Sixty-eight (61F, 7 M) patients, with normal baseline cardiac function, was included. Chemotherapy combinations contained either Dox or epirubicin as 1st line chemotherapy. Systolic and diastolic cardiac functions were evaluated before and after therapy (mean follow-up:10.4$\pm$4.7 months) using E and SPECT. Left ventricular ejection fraction (EF), peak filling rate (PFR), peak ejection rate (PER), end systolic volume (ESV), end diastolic volume (EDV) values were calculated using SPECT data. GSTP1 and CBR3 polymorphisms were analyzed using TaqMan probes.
Results: The mean received anthracycline dose was 508$\pm$153 mg/m^2 (210–1188). Fifteen patients (28%) received adjuvant radiotherapy over the cardiac region. HER2 antagonists were given in 7 patients after chemotherapy. EF values were significantly decreased after AC with both SPECT and E ($p < 0.01$, $p = 0.043$). In 1 patient EF was below 40% after 7 months at 600 mg/m^2 of Dox ESV ($p = 0.028$) and diastolic parameters; mitral inflow e wave deceleration time ($p < 0.001$), mitral inflow colour propagation ($p = 0.001$), and PFR ($p = 0.038$) deteriorated significantly after therapy. Patients who received HER2 antagonists and radiation to cardiac region, showed higher ESV % change ($p = 0.015$, 0.013) compared to others. AA genotype of GSTP1 revealed higher ESV% increase (AA genotype: 9.4 ml $\pm$10; G allele carriers: 3.09 ml $\pm$ 10) after AC ($p = 0.02$). No statistically significant difference between cardiac parameters and CBR3 polymorphism genotypes were found.
Conclusion: This prospective clinical study showed a significant relationship between GSTP1 polymorphism and ESV change after Dox treatment. In the future we plan to increase the number of the patients of this study.

1074 POSTER

Feature of improvement of hormonal therapy: an action code

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Background: Manipulation of the hormonal environment affects breast tumor growth in many species but only never eliminates the tumor completely. Research on influence of a hormonal background on growth and ER status of mice mammary tumors opens a new variants of hormonal therapy.
Methods: The levels of ER were determined by means of the dextran-coated charcoal technique. The resulting data were analyzed by a saturation curve and a Scatchard plot. Tumor transplantation.
Results: On a mouse model it is established, that growth of a tumor at cyclically changing a hormonal level leads to heterogeneity ER status of mammary tumors that complicates hormone therapy. At the same time, continuous influence of such substances as steroid hormones, reserpine, retinol, chorionic gonadotropin results in reduction of value standard deviation growth of tumors in mice. It is established also that continuous application of estradiol leads to homogenization of the estrogen receptor status of mice mammary tumor. Nevertheless, the moment of occurrence of spontaneous tumors is not adequately studied. The results obtained to date suggest that tumor cells may originate in C3H/Sn mice shortly after pairing. Both the originating of tumors and a breeding equally depends on seasons. I obtained data confirm a greater role of steroid hormones and stress for initialization of tumor formation and modulation of its properties. The ability of tumor cells to adapt for change of surrounding microenvironment answers on a question on a paradoxicality of a hormone therapy. Series of tumor parameters such as the invasiveness, heterogeneity, etc. are a consequence of adaptive properties of a tumor cells. Based on experimental methods of research conclusions which can promote improvement of treatment by means of existing methods are received.
Conclusions: Steroid hormones have many advantages to their choice as a medicine against a cancer: a) simple substances freely getting into cells; b) tumor cells of mammary gland answer to low (physiological) concentration; c) influence on a transcription of genes; d) low cost; e) there are natural analogies of application for reprogramming of cell state. The last explains why the effective remedy against a cancer until now is not found. Reprogramming of cells cannot be carried out by one substance or for one act of actions. Serial influence is a code which demands more time for decoding.

Poster presentations (Mon, 21 Sep, 09:00−12:00)
Translational research

1075 POSTER

Sphingosine kinase 1 inhibition sensitizes hormone-resistant prostate and breast cancer cells to docetaxel

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Background: It has recently been shown that docetaxel chemotherapy is effective in prolonging life in patients with prostate cancer (PCa). We have investigated potential ways of increasing the effectiveness of chemotherapy in this disease. We have previously reported that sphingosine kinase 1 (SphK1) inhibition is a key step in docetaxel-induced apoptosis in hormono-refractory PCa cells (Pchejetski, Golzio et al. 2005) and that pharmacological SphK1 inhibition is chemosensitizing in the docetaxel-resistant androgen-sensitive PCa cells (Pchejetski, Doumerc et al. 2008).
Material and Methods: In this current study we have addressed the mechanism of docetaxel-induced apoptosis of PC-3 PCa and MDA-MB 231 breast cancer (BCa) cells and evaluated the synergetic profile of specific SphK1 inhibitors.
Results: Using both PCa and BCa cells we have first identified SphK1-dependent and -independent components of docetaxel induced apoptosis, where SphK1 inhibition is critical for increased docetaxel efficacy. Furthermore we have shown that SphK1 inhibition by docetaxel is a two-step process involving an initial loss of enzyme activity followed by a decrease in SphK1 gene expression. We have demonstrated that both pharmacological and siRNA-mediated SphK1 inhibition leads to a four-fold decrease in the docetaxel IC50 dose.
Conclusions: This work points out to potential ways of increasing the effectiveness of chemotherapy for prostate and breast cancer by SphK1 inhibition.