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6. Ryzhakova O.S., Solovyeva N.I.

Matrix metalloproteinases (MMP) - MMP-1,-2,-9 and its endogenous activity regulators in transformed by E7 oncogene HPV16 and HPV18 cervical carcinoma cell lines.

Matrix metalloproteinases (MMP) play a key role in development of tumor invasion and metestasis. The purpose of the work is the elucidation of peculiarities of expression of MMP-1, MMP-2, MMP-9 and their activity regulators: plasminogen activator uPA and tissue inhibitors of MMPs - TIMP-1 and TIMP-2 in human cell lines of squoamous cell carcinoma (SCC). Comparative study of MMPsâ€™ expression was carried out on cell lines SCC which differed in HPV types (HPV-16 and HPV-18): SiHa, Caski â€“ Ð•Ð V16, Hela, Ð¡4-1 â€“ HPV18). As a control, the Ð¡33Ð• line was used where HPV copies were absent. The human papilloma viruses (HPV) of high risk â€“ HPV-16, HPV-18, as etiological factors of initiation of cervical cancer, are most widespread and most aggressive among oncogenic HPVs. Study of MMP expression involved estimation of expression of mRNA using the RT-PCR method and determination of collagenolytic activity by hydrolysis of fluorogenic type 1 collagen and also by the zymography method. It was shown that: 1. In both types of cell lines, the MMP-1 expression was essentially increased (2 to 8 times), and in HPV18 lines it was most expressed. The exception was made by the SiHa line in which the decrease of expression of this enzyme was observed. MMP-2 expression was at the control level in both types of cell lines. 2. Expression of inhibitors generally was at the control level. The only exception was the C4-1 line where the expression of TIMP-1 and TIMP-2 was increased in 1,7 and 2,6 times accordingly. Expression of uPA was increased 2 to 4,5 times in all cell lines except Siha where was lowered to 20%. 3. Collagenolytic activity in the Caski and Hela cell line was 2-3 times higher that it was in control, while the activity in the SiHa cell line was compatible with that in the control. Research of gelatinolytic activity also as well as the data on an expression Ð¼Ð Ð•Ðš has revealed only presence ÐœÐœÐŸ-2, but not ÐœÐœÐŸ-9 in all cervical carcinoma cell lines. The data obtained provide evidence for a significant disturbance in transformed cells of enzyme/inhibitor/activator ratio â€“ which occurs, for the most part, at the cost of elevated expression of MMP-1 and its activator whereas the expression of MMP-2 and inhibitors remains virtually unchanged, which leads to the increase of the destructive potential of transformed cells.

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7. Gorbenko M.V., Popova T.N., Shulgin K.K., Popov S.S.

The activity of glutathione antioxidant system at melaksen and valdoxan action under experimental hyperthyroidism in rats.

Investigation of glutathione antioxidant system activity and diene conjugates content in rats liver and blood serum at the influence of melaksen and valdoxan under experimental hyperthyroidism (EG) has been revealed. It has been established that the activities of glutathione reductase (GR), glutathione peroxidase (GP) and glutathione transferase (GT), growing at pathological conditions, change to the side of control value at these substunces introduction. Reduced glutathione content (GSH) at melaxen and valdoxan action increased compared with values under the pathology, that, obviously, could be associated with a reduction of its spending on the detoxication of free radical oxidation (FRO) toxic products. Diene conjugates level in rats liver and blood serum, increasing at experimental hyperthyroidism conditions, under introduction of melatonin level correcting drugs, also approached to the control meaning. Results of the study indicate on positive effect of melaxen and valdoxan on free radical homeostasis, that appears to be accompanied by decrease of load on the glutathione antioxidant system in comparison with the pathology.

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8. Gorozhanskaya E.G., Sviridova S.P., Dobrovolskaya M.M., Zubrikhina G.N., Kashiya S.R.

Selenium and oxidative stress in cancer patients.

In order to identify the features of violations of free-radical processes in blood serum of 94 untreated cancer patients with different localization of the tumor (cancer of the stomach, colon, breast, ovarian, hemoblastoses) were determined selenium levels and indicators of oxidative stress (sum of metabolites of nitrogen - NOx, the level of superoxide dismutase - Cu/ZnSOD and malondiialdehyde-MDA, and the activity of catalase). In addition, 40 patients with malignant liver disease and clinical signs of liver failure in the early postoperative period was carried out a comparative evaluation of the efficacy of selenium-containing drug 'Selenaze' (sodium selenite pentahydrate). It was found that selenium levels in cancer patients by 25-30% below the norm of 110-120 mg/l at a rate of 73.0Â±2.6 mg/l. Low levels of NOx was detected in patients with all tumor localizations (22.1Â±1.1 mM, with normal range 28.4Â±0.9 mM). The exceptions were patients with extensive malignant process in the liver, in which the NOx levels were significantly higher than normal (p<0.001). The high level of NOx has a toxic effect on the hepatocyte, causing metabolic disorders and inflammatory-necrotic changes in the liver. Elevated levels of SOD and MDA in normal values of catalase activity was detected in all patients. The use of 'Selenaze' in postoperative patients with tumors of the liver increased selenium levels by 10-12%, which was accompanied by a decrease in the content of SOD and NOx, and contributed to earlier recovery of detoxic and synthetic liver function. These findings point to an intensification of oxidative stress and metabolic disorders in the malignant process, which is the basis for metabolic correction.

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9. Lotosh N.Y., Selishcheva A.A., Nadorov S.A., Badyshtov B.A., Volkov I.E., Saveljev S.V.

The proinsulin level in the blood of children with type 1 diabetes mellitus of various duration.

Proinsulin content was measured in the serum of 82 children (aged from 3 to 14 years) with type 1 diabetes mellitus of various duration. Three groups of patients characterized by low (54%), normal (42%) and high (4%) levels of this prohormone were recognized. No dependence the proinsulin level on the disease term was found. The serum proinsulin level may be used as a parameter specifying the pathogenesis of type 1 diabetes mellitus.

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10. Zhloba A.A., Subbotina T.F., Lupan D.S., Bogova V.A., Kusheleva O.A.

Arginine and lysine as products of basic carboxypeptidase activity associated with fibrinolysis.

Blood carboxypeptidases play an important role in the regulation of fibrinolysis. We have proposed here the method for the assay of blood carboxypeptidase activity associated with coagulation/fibrinolysis using the natural substrate fibrin and the detection of basic amino acids arginine and lysine as products in the conditions close to those in vivo . Plasma samples from 15 patients with arterial hypertension were investigated. The coagulation and subsequent fibrinolysis were initiated by addition of standard doses of thrombin and tissue plasminogen activator, respectively. Arginine and lysine concentrations before, during, and after completion of fibrinolysis were determined using HPLC. The parameters of fibrinolysis were evaluated by clot turbidity assay. Fibrinolysis led to a large and significant increase in concentrations of arginine and lysine in the incubation mixture by 101 and 81%, respectively. The duration of fibrinolysis initiation significantly correlated to the degree of increase of these amino acids: r =-0.733 Ð¸ -0.761 for arginine and lysine, respectively (p<0.05). The rates of amino acids liberation during fibrinolysis demonstrate different pattern: arginine generation had two maximums: at the beginning of clot lysis and at his end, whereas the liberation of lysine occurred mainly at the middle of fibrinolysis. Thus, the carboxypeptidase activity associated with fibrinolysis can be considered as a local source of the essential aminoacids.
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11. Lesnichenko I.F., Gritsaev S.V., Sergeev A.N., Kostroma I.I., Tiranova S.A.

Activity of matrix metalloproteinases MMP-2 and MMP-9 in bone marrow plasma of patients with acute myeloid leukemia.

Prognostic significance of the ratio of MMP-2 and MMP-9 activities (MMP-2/MMP-9) have been investigated in bone marrow plasma (BMP) of 53 patients with acute myeloid leukemia (AML) using the method of zymography. During BMP collection 33 patients were diagnosed with complete remission (CR) and 22 patients without CR. The ratio MMP-2/MMP-9 was approximately 1.00 (the upper limit was equal 1.77) in the 75% of patients. At the same time the ratio was more than 3 times higher in 13 patients (25%): their minimal value was 1.80 (p<0.001). In the group with high ratio MMP-2/MMP-9 only 3 patients were with CR, and 10 patients with resistant variant of AML. The median of the overall survival (OS) of these 10 patients was significantly lower than OS of other investigated AML patients (7.0 vs 33.5 months Ñ€<0.001). Thus the high MMP-2/MMP-9 ratio (Â³1.8) may be associated with unfavorable course of AML.
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12. Sanzhakov M.A., Prozorovskyi V.N., Ipatova O.M., Tikhonova E.G., Medvedeva N.V., Torkhovskaya T.I.

Drug delivery system on the base of phospholipid nanoparticles for rifampicin.

Low bioavailability of rifampicin, one of the main antituberculous drug, stimulates searches of its new optimized formulations. The present study has showen possibility of rifampicin embedding into nanoparticles from plant phosphatidylcholine (diameter of 20-30 nm). Addition of sodium oleate to the phospholipid system caused a 2-fold increase of the percent of rifampicin incorporation. After oral administration to rats, the maximal drug observed in plasma one hour after was 0.5 and 4.2 mkg/ml for free rifampicin for rifampicin in phospholipids-oleate nanoparticles, respectively. These levels were maintained for more than two hours of the experiment. High rifampicin bioavailability in the oleate containing phospholipid nanosystem suggests prospectivity of its pharmaceutical elaboration.
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13. Fedyushkina I.V., Romero Reyes I.V., Lagunin A.A., Skvortsov V.S.

Mode of action prediction of ligands of steroid hormone receptors.

The several predictive models based on two well-known methods PASS and SIMCA were created. These models predict a type of physiological response of steroid compounds binding to nuclear receptors of steroid hormones. We considered 10 variants: the agonists and the antagonists of estrogen, progesterone, androgen, glucocorticoid and mineralocorticoid receptors respectively. Two different sets of descriptors were used during SIMCA (the Dragon descriptors and indices of similarity). The results of discriminant analysis are good enough with average accuracy of 80-85%.
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