

1. Tamkovich S.N., Voytsitskiy V.E., Laktionov P.P.

Modern approach of breast cancer diagnostics.

In the review have been classified literature data concerning modern instrumental, microscopic and molecular (metabolomics, proteomics, genetics and epigenetics) approaches for early breast cancer diagnostics. The analytical performance and perspectives of their application in clinical practice also have been evaluated.

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2. Raevsky O.A., Solodova S.L., Lagunin A.A., Poroikov V.V.

Computer modeling of blood brain barrier permeability of physiologically active compounds.

At present work discusses the current level of computer modeling the relationship structure of organic compounds and drugs and their ability to penetrate the BBB. All descriptors that influence to this permeability within classification and regression QSAR models are generalized and analyzed. The crucial role of H-bond in processes both passive, and active transport across BBB is observed. It is concluded that further research should be focused on interpretation the spatial structure of a full-size P-glycoprotein molecule with high resolution and the creation of QSAR models describing the quantitative relationship between structure and active transport of substances across BBB.

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3. Shaturny V.I., Shakhidzhanov S.S., Sveshnikova A.N., Panteleev M.A.

Activators, receptors and signal transduction pathways of blood platelets.

Platelet participation in hemostatic plug formation requires transition into an activated state (or, rather, variety of states) upon action of agonists like ADP, thromboxane A₂, collagen, thrombin, and others. The mechanisms of action for different agonists, their receptors and signaling pathways associated with them, as well as the mechanisms of platelet response inhibition are the subject of the present review. Collagen exposed upon vessel wall damage induced initial platelet attachment and start of thrombus formation, which involves numerous processes such as aggregation, activation of integrins, granule secretion and increase of intracellular Ca²⁺. Thrombin, ADP, thromboxane A₂, and ATP activated platelets that were not initially in contact with the wall and induce additional secretion of activating substances. Vascular endothelium and secretory organs also affect platelet activation, producing both positive (adrenaline) and negative (prostacyclin, nitric oxide) regulators, thereby determining the relation of activation and inhibition signals, which plays a significant role in the formation of platelet aggregate under normal and pathological conditions. The pathways of platelet signaling are still incompletely understood, and their exploration presents an important objective both for basic cell biology and for the development of new drugs, the methods of diagnostics and of treatment of hemostasis disorders.

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4. Lokhov P.G., Maslov D.L., Trifonova O.P., Balashova E.E., Archakov A.I.

Mass spectrometry of blood low-molecular fraction as a method for unification of therapeutic drug monitoring.

The article describes a new therapeutic drug monitoring (TDM) method based on direct infusion of low-molecular fraction of blood into electrospray ionization source of mass spectrometer. This technique allows performing TDM of almost all drugs used in clinic. In article, the universality and high-throughput of the method, that significantly simplifies its wide application, have been shown. Moreover, the possibility of method application in most cases of drug therapy has been argued as a tool of control of drug doses, rationality of drug therapy, and the quality of the drugs themselves. In conclusion, the prospects for application of the method as primary means of improving the quality and personalization of drug therapy have been discussed.

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5. Shumyantseva V.V., Makhova A.A., Bulko T.V., Shich E.V., Kukes V.G., Usanov S.A., Archakov A.I.

Role of antioxidants in electro catalysis of cytochrome P450 3A4.

The electrochemical analysis of cytochrome P450 3A4 catalytic activity has shown that vitamins C, A and E influence on electron transfer and Fe³⁺/Fe²⁺ reduction process of cytochrome P450 3A4. These data allow to assume possibility of cross effects and interference of vitamins-antioxidants with drugs metabolised by cytochrome P450 3A4, at carrying out of complex therapy. This class of vitamins shows antioxidant properties that lead to increase of the cathodic current corresponding to heme reduction of this functionally significant haemoprotein. Ascorbic acid of 0.028-0.56 mM concentration stimulates cathodic peak (an electrochemical signal) of cytochrome P450 3A4. At the presence of diclofenac (Voltaren) - a typical substrate of cytochrome P450 3A4 - the increase growth of a catalytic current testifying to an electrocatalysis and stimulating action of ascorbic acid is observed. In the presence of vitamins A and E also is registered dose-dependent (in a range of 10-100 M) increase in a catalytic current of cytochrome P450 3A4: the maximum increase corresponds to 229 ± 20% for 100 M of vitamin A, and 162 ± 10% for 100 M of vitamin E. Vitamin E in the presence of P450 3A4's inhibitor itraconazole doesn't give essential increase in a reductive current, unlike retinol (vitamin A). This effect can manifest substrate properties of tocopherol (vitamin E). The electrochemical approach for the analysis of catalytic activity of cytochrome P450 3A4 and studies of influence of biologically active compounds on an electrocatalysis is the sensitive and effective sensor approach, allowing to use low

concentration of protein on an electrode (till 10-15 mol/electrode), to carry out the analysis without participation of protein redox partners, and to reveal drug-drug or drug-vitamins interaction in pre-clinical experiments.

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6. *Miroshnichenko I.I., Platova A.I., Safarova T.P., Yakovleva O.B.*

Determination of homocysteine by lc-ms-ms with atmospheric pressure chemical ionization.

Homocysteine (Hcy) is an intermediate of methionine metabolism. High plasma Hcy concentrations are an independent risk factor for stroke, peripheral vascular disease, deep venous thrombosis, coronary disease, and cognitive deficiency. Apparently, it is a great importance to measure Hcy levels in human blood. A new method for the quantification of Hcy by means of reversed-phase LC/atmospheric pressure chemical ionization mass spectrometry has been developed. The MRM ion transition, m/z 136.0 \hat{A} @ 90.0 was used for Hcy quantification. The limit of detection was 0.4 mM, quantification was performed from 1 mM to 40 mM with coefficient of determination of $R^2=0.997$. The method was applied successfully to Hcy determination in human blood.

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7. *Yuryeva K.S., Nevskaya K.V., Dzuman A.N., Ikkert O.P., Ivanov V.V., Saltikova I.V., Sazonov A.E., Ogorodova L.M.*

Stimulation of adenosine receptors on myeloid cells enhance leukocyte migration at the site of burn injury.

Adenosine, endogenous purine nucleoside, is an ATP metabolite that also acts as an extracellular signaling molecule. The concentration of extracellular adenosine rises during hypoxia and cell damage leading to numerous pleiotropic effects. Although a high concentration of adenosine was found at burn injury, the effect has not been well elucidated. We have studied human peripheral blood myeloid cell, due to their expression of specific adenosine receptors and capacity to migrate to the site of burn injury. We have shown that myeloid cells after 72 hours of stimulation of adenosine receptors develop altered expression of surface antigens: preserved monocyte \hat{A} ™s marker CD14 with already expressed dendritic cell markers (CD209, CD1a). Whereas untreated cells have already lost monocyte marker in 72 hours, and express CD1a more abundantly. Adenosine modified myeloid cells express also higher levels of mRNA of proinflammatory cytokines and chemoattractants (IL-6, IL-8, IL-1 b). Using mouse model of the burn injury we have shown, that adenosine modified bone marrow derived myeloid cells injected in the site of the injury promote migration of granulocytes, monocytes, macrophages, and fibroblasts on the 7th day after burn. Thus, stimulation of adenosine receptors alters differentiation and function of myeloid cells. In the site of burn injury adenosine modified myeloid cells augment cell migration due to paracrine factors.

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8. *Karpova I.V., Mikheev V.V., Marysheva V.V., Bychkov E.R., Shabanov P.D.*

Effect of acute hypoxia with hypercapnia on the content of monoamines in symmetrical brain structures of the BALB/c male mice.

The changes in activity of monoaminergic systems of both the right and the left brain hemispheres of the BALB/c male mice after an acute hypoxia with hypercapnia were studied. The concentrations of dopamine, serotonin and their metabolites dihydroxyphenylacetic, homovanilic and 5-hydroxyindolacetic acids were measured by HPLC in the brain cortex, hippocampus and striatum of the right and the left hemispheres. The more high concentration of serotonin was revealed only in the cortex of the left hemisphere in control mice without hypoxia with hypercapnia. The asymmetry in dopamine level was not registered in all structures studied. Acute hypoxia with hypercapnia decreased the dopamine level in the striatum and the serotonin level both in the hippocampus and the brain cortex. The dopamine metabolites level was reduced in the striatum and in the brain cortex of hypoxed mice: both metabolites in the right brain cortex and only dihydroxyphenylacetic acid in the left brain cortex. Serotonin metabolism was decreased in all brain structures studied after hypoxia with hypercapnia in mice. Therefore, serotonergic system of the brain is more sensitive to acute hypoxia with hypercapnia than dopaminergic system.

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9. *Kulieshova D.K., Davydov V.V.*

Some peculiarities in the manifestation of oxidative stress and current status of antioxidant system in adolescents of different age groups with obesity, complicated by insulin resistance and without it.

The study has shown that neuroendocrine obesity in adolescents is associated with the formation of oxidative stress which is more pronounced in early than in late puberty. Obesity with concomitant insulin resistance increases manifestations of oxidative stress accompanied by a compensatory increase in the activity of catabolic enzymes and reduced capacity of the defense antioxidant system in late puberty. These alterations may be caused by age-related changes in hormonal secretion under conditions of insulin resistance in late puberty.

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