

1. *Chetina E.V., Markova G.A.*

Upcoming value of gene expression analysis in rheumatology.

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology, which involves disturbance in immune system signaling pathway functions, damage of other tissues, pain and joint destruction. Modern treatment attempts to improve pathophysiological and biochemical mechanisms damaged by the disease. However, due to the RA patient heterogeneity personalized approach to treatment is required; the choice of personalized treatment is complicated by the variability of patient's response to treatment. Gene expression analysis might serve a tool for the disease control and therapy personification for inhibition of inflammation and pain as well as for prevention of joint destruction.

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2. *Vakhrushev I.V., Novikova S.E., Tsvetkova A.V., Pyatnitskiy M.A., Yarygin K.N.*

Comparative proteomic profiling of nuclear and cytosolic fractions from cell lines of different origin.

Proteomic analysis of the nuclear fraction is of great importance, since many cellular processes are initiated in the nucleus. Refinement and choice of experimental procedures for cell lysate fractionation and parameters for mass spectrometric detection and data processing continue to be of current interest. The mass spectrometry analysis presented here was tested on human cell lines derived from different tissues: HL-60 (peripheral blood); HepG2 (liver); EA.hy926 (vascular endothelium). High reproducibility of results and their consistency with biological properties of the objects under study were demonstrated. The use of cells of different types made it possible to reveal a set of 16 proteins whose LFQ-values allow for the discrimination between proteome fractions regardless of cell origin. Also, a set of 16 proteins is suggested which are associated with individual characteristics of cell lines regardless of cell fraction. These protein panels can serve as parameters to verify the proteomic analysis done was of sufficient quality, in particular as indicators of successful fractionation of cell or tissue lysate.

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3. *Kakorin P.A., Babenkova I.V., Teselkin Y.O., Ramenskaya G.V., Demura T.A., Kukes V.G.*

Hepatoprotective activity of aqueous extract from *Caragana jubata* (Pall.) Poir. shoots in the model of acute hepatitis induced by acetaminophen in rats.

The aim of the study was to investigate the hepatoprotective activity of an aqueous extract of *Caragana jubata* (Pall.) Poir. Acute experimental hepatitis was induced by acetaminophen administration of 1000 mg/kg. Studies were conducted in white Wistar rats. The aqueous extract of *C. jubata* demonstrated the hepatoprotective effect, comparable to that of the reference preparation "Carcil". This was manifested by the normalization of biochemical blood parameters (ALT, AST, alkaline phosphatase, cholesterol, total bilirubin) and antioxidant activity of liver homogenates, determined by the method based on oxidation of luminol induced by 2,2'-azobis(2-amidinopropane). Normalization of morphofunctional indices was also shown in a histological study of liver of rats that received aqueous extract from *C. jubata*.

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4. *Mikurova A.V., Skvortsov V.S.*

Creation of a generalized model prediction of inhibition of neuraminidase of influenza virus of various strains.

Preliminary results of construction of overall model for prediction of IC50 value of ligands of influenza virus neuraminidase of any strain are presented. We used MM-PBSA (MM-GBSA) energy terms calculated for the complexes obtained after modeling of 30 variants of neuraminidase structures, subsequent docking and simulation of molecular dynamics as independent variables in prediction equations. The structures of known neuraminidase-inhibiting drugs (oseltamivir, zanamivir and peramivir) and a neuraminidase substrate (MUNANA) were used as ligands. The correlation equation based on calculated energetic parameters of inhibitor complexes with neuraminidase did not result in the prediction of IC50 with acceptable parameters ($R^2 \approx 0.3$). However, if information about binding energy of the substrate used for neuraminidase assay (and IC50 detection) is included the resulting IC50 prediction equations become significant ($R^2 \approx 0.55$). It is concluded that models based on IC50 values as a predictable variable and combining information about binding of different ligands to different variants of the target proteins must take into account the binding properties of the substrate (used for IC50 determination). The predictive power of such models depends critically on the quality of the modeling of the ligand-protein complexes.

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5. *Kudinov V.A., Zakharova T.S., Torkhovskaya T.I., Kashirtseva V.A., Morosevich G.E., Ipatova O.M., Archakov A.I.*

Improving of HDL capacity for macrophages cholesterol efflux after plasma incubation with phospholipid nanoparticles.

In connection with recent data about antiatherogenic importance of not only plasma HDL concentration, but of their cell cholesterol efflux capacity as well, the possibility of its correction by phospholipid (PL) nanoparticles was studied. Blood plasma was incubated with earlier elaborated PL nanoparticles emulsion with the particle diameter up to 30 nm, and HDL cholesterol efflux capacity of apo B-depleted plasma was studied. Using macrophages THP-1 preloaded 3H-cholesterol were used. The addition of incubated plasma supernatants with the elevated PL/apo A-1 ratio to cell media resulted in almost increase in two fold 3H-cholesterol efflux as compared with native HDL. The maximal efflux was observed at the PL/apo A-1

ratio of 1.06 as compared with native apo B-depleted plasma (the PL/apo A-1 ratio of 0.85). Results suggest possible usage of ultrasmall PL nanoparticles for regeneration of impaired antiatherogenic HDL functionality. This approach seems to be predominant compared with the usage of PL emulsions with detergent or apoprotein A1.

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6. *Karpova I.V., Mikheev V.V., Marysheva V.V., Kuritsyna N.A., Popkovskii N.A., Bychkov E.R., Shabanov P.D.*

The effect of acute hypoxia with hypercapnia on the content of monoamines in symmetrical areas of the brain in albino mice.

Changes in the activity of monoaminergic systems of the left and right hemispheres of the brain after acute hypoxia with hypercapnia were investigated in male albino mice. The concentrations of dopamine (DA), serotonin (5-HT) and their metabolites dihydroxyphenylacetic (DOPAC), homovanilic (HVA) and 5-hydroxyindolacetic (5-HIAA) acids were measured by HPLC in the brain cortex, hippocampus and striatum of the right and the left hemispheres. In the control mice not exposed to hypoxia with hypercapnia, a higher concentration of DA in the left cortex was detected. No asymmetry in the content of other substances has been identified in the investigated structures. Acute hypoxia with hypercapnia led to the right-sided increase of DA and 5-HT levels and to the left-sided reduction of DOPAC in the cerebral cortex. Under the condition of hypoxia with hypercapnia, in the hippocampus, the left-sided increase of the DA content was revealed. In the striatum the contents of monoamines and their metabolites were insignificantly changed. It has been concluded that acute hypoxia with hypercapnia causes asymmetric changes in monoaminergic systems of the archicortex and the neocortex.

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7. *Gorina E.I., Popova T.N., Shulgina K.K., Popov S.S., Panchenko L.F., Safonova O.A.*

The effect of biguanide derivatives on oxidative stress in rats with hyperglycemia.

The effect of the synthetic biguanide derivatives N-[imino(1-piperidyl)methyl]guanidine (NIPMG) and 1,3-dimethyl-5-[(carbamidamidomethanimidoil)amino]benzoyl-1,3-dicarboxylate (DCB) on the degree of proteins oxidative modification (POM) and the DNA fragmentation, the content of the lipid peroxidation primary products α,β -conjugated dienes (CD), and the activity of glutathione antioxidant system in the liver and heart of rats with experimental hyperglycemia was investigated. Administration of the biguanides (15.0 mg/kg) to hypoglycemic rats promoted reduction of the free radical processes intensity in the studied tissues. Data about CD and POM level changes in hyperglycemic rats treated by NIPMG and DCB correlate with the results of DNA fragmentation degree evaluation. At the same time, the activity of antioxidant enzymes (glutathione peroxidase and glutathione reductase), and the reduced glutathione content in the liver and heart of rats changed toward control values. For metformin, which was used as a comparison drug, changes in the studied parameters in the same direction were also found. These results indicate the ability of the tested biguanide derivatives to exhibit a positive regulatory effect on free radical homeostasis, reducing the degree of oxidative stress at this pathology.

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8. *Stvolinsky S.L., Antonova N.A., Kulikova O.I., Lopachev A.V., Abaimov D.A., Al-Baidani I., Lopacheva O.M., Fedorova T.N., Kaplun A.P., Sorokoumova G.M.*

Lipoilcarnosine: synthesis, study of physico-chemical and antioxidant properties, biological activity.

Synthesis of lipoilcarnosine (LipC) – a conjugated molecule based on two natural antioxidants, carnosine and α -lipoic acid, is described. Its physico-chemical, antioxidant properties and biological activity are characterized. According to reversed-phase HPLC with a UV detector, purity of the final product was 89.3%. The individuality of the obtained sodium salt of LipC was confirmed by tandem HPLC-mass spectrometry. High resistance of LipC to hydrolysis with serum carnosinase was demonstrated. The antioxidant activity of LipC measured by reaction with the formation of thiobarbituric acid reacting substances and kinetic parameters of iron-induced chemiluminescence was higher than that of carnosine and lipoic acid. LipC did not affect viability of SH-SY5Y human neuroblastoma culture cells, differentiated towards the dopaminergic type, at concentrations not exceeding 5 mM. At the concentration range of 0.1-0.25 mM LipC protected neuronal cells against 1-methyl-4-phenylpyridinium (MPP⁺)-induced toxicity.

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9. *Barinova K.V., Melnikova A.K., Schmalhausen E.V., Muronetz V.I.*

A rational approach to obtaining high-specific polyclonal antibodies against recombinant alpha-synuclein.

The approach for the quick and efficient production of polyclonal antibodies to the target antigen alpha-synuclein has been proposed. Two methods have been employed to purify specific rabbit polyclonal antibodies against recombinant human alpha-synuclein, produced by subcutaneous immunization with complete Freund's adjuvant. It was shown that purification on CNBr-activated Sepharose with immobilized alpha-synuclein resulted in antibody preparation with rabbit serum histidine-rich glycoprotein as a contaminant. Two-stage antibody purification procedure – first on Sepharose with immobilized protein G, and then on alpha-synuclein immobilized column helps to avoid contamination and to obtain homogenous antibody preparation. Antibodies recognize different conformations of alpha-synuclein and can be used in a variety of immunochemical approaches, including immunocytochemistry.

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10. *Plotnikova E.A., Grin M.A., Ostroverkhov P.V., Pantushenko I.V., Yakubovskaya R.I., Kaprin A.D.*

Primary screening of substances-photosensibilizers of the bacteriochlorin range for photodynamic therapy of malignant neoplasms.

This paper presents a primary screening of bacteriochlorin-type compounds with aminoamide, propyl and carbohydrate substituents aimed for development of a new generation photosensitizers (PS) for photodynamic therapy of malignant tumors. Absorption and fluorescence spectral characteristics of the compounds, their storage stability in solutions under dark conditions and light exposure, photo-induced and dark cytotoxicity against human HEP2 tumor cells have been studied. It has been shown that the dyes with aminoamide substituents have an absorption maximum at 754 ± 2 nm in the long wavelength region and they are not stable during storage (the specific fluorescence intensity decreased by 33-56% during 24 hours). The long wavelength region absorption of the propyl and carbohydrate substituted compounds varied in the range 780-831 nm, they were stable

in solutions during storage and under light irradiation. Except the dye with a carbohydrate residue in the exocycle E, all PS exhibited the high photo-induced activity and low level of the dark cytotoxicity. The highest photo-induced cytotoxicity was observed for compounds with aminoamide substituents in the macrocyclic ring (IC 50 values ranged from 17 nM to 49 nM after 2 hour incubation with PS followed by exposure to the 10 J/cm² dose of red light). Taking into account the totality of the physico-chemical and biological properties, as well as manufacturability of production, O-propyloxime-N-propoxybacteriopurinimide methyl ester was chosen as the most promising candidate compound for further investigations.
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11. Pogorelova T.N., Nikashina A.A., Gunko V.O., Larichkin A.V., Chebotarev D.A.

Features of redox processes in the amniotic fluid at placental insufficiency.

Activity of prooxidant enzymes (NADPH-oxidase and xanthine oxidase), antioxidant enzymes (superoxide dismutase (SOD) and catalase), enzymes of the glutathione-dependent systems, as well as antioxidant vitamins (retinol and alpha-tocopherol), lipid peroxidation products (LPP) (conjugated dienes and Schiff bases), and peroxide chemiluminescence were studied in the amniotic fluid at different periods of physiological pregnancy and placental insufficiency (PI). It was found that at PI the activity of NADPH-oxidase, xanthine oxidase increased and the activity of SOD, catalase, glutathione peroxidase, glutathione reductase, glutathione transferase and the content of fat-soluble vitamins decreased. The direct and inverse correlation between the studied pro- and antioxidant parameters and the content of LPP products, was found to be different in the II and III trimesters of gestation. The revealed differences obviously reflect metabolic impairments in the fetoplacental complex, and the activity and level of the parameters of redox processes can be used as tests for pre- and postnatal disorders.

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