

1. *Moskaleva N.E., Zgoda V.G.*

Current methods of cytochrome P450 analysis.

Current review describes recent approaches of cytochrome P450 concentration and activity evaluation. Special attention paid to modern methods of proteomic analysis such as electrophoresis and chromatography-mass-spectrometry. Methods of targeted proteomic applicable for quantitative and qualitative study of P450s in biological samples as well as methods for the enzyme activity measurements are reviewed. Finally, data on correlation between certain P450 isoform content and its specific enzymatic activities were described and discussed in the review.

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2. *Ivanov S.D.*

Biochemical markers predicting response to radiation- and radiochemo-therapy in cancer patients.

In last years there is increasing interest in radiogenomics and the characterization of DNA array molecular profiles that can predict tumor and no tumor tissues radioresponse. Ongoing studies carried out worldwide in the banking of tumor and no tumor samples give evidence that perspective markers for response prediction in individual patient to intended radiation therapy can be some apoptotic indexes, spectrum a number of specific proteins, and DNA-based microarray molecular profiling analysis as well determination of single nucleotide polymorphisms in genome of the patients. So far there are only a few robust reports of molecular markers predicting tumor and no tumor tissues response to radiation. The results of new studies, which in future should be validated in larger definitive trials, are likely to see in nearest years. It is needed to determine technologies of methods and to define more precisely areas of its applications.

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3. *Chernikov V.A., Gorokhovets N.V., Savvateeva L.V., Severin S.E.*

Analysis of complex formation of human recombinant hsp70 with tumor-associated peptides.

Molecular chaperones of HSP70 family assists presentation of exogenous antigenic peptides by antigen-presenting cells (APC). HSP70-peptide complexes are powerful immunotherapeutic agents, which enhance cross-presentation of captured antigen in dendritic cells and macrophages. Several clinical trials have shown that HSP-based cancer vaccines possess good efficacy and safety. However, sometime it is impossible to isolate sufficient amount of vaccine. These make us to pay attention for recombinant HSP70-based vaccines and to optimize in vitro complex formation mechanism. Here we have investigated two human recombinant proteins HSP70HYB and HSC70. Optimal values of ADP concentration, pH, temperature and peptides excess are determined in this work. We have also shown that proposed complex formation method enriches eluted from HSP70-complexes peptide repertoire compared to in vivo assembled ones.

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4. *Kudryavtsev V.A., Makarova Y.M., Kabakov A.E.*

Thermosensitization of tumor cells with inhibitors of chaperone activity and expression.

Effects of inhibitors of the heat shock protein 90 (HSP90) chaperone activity and inhibitors of the heat shock protein (HSP) expression on sensitivity of HeLa tumor cells to hyperthermia were studied. It was found that nanomolar concentrations of inhibitors of the HSP90 activity (17AAG or radicicol) slowed down chaperone-dependent reactivation of a thermo-labile reporter (luciferase) in heat-stressed HeLa cells and slightly enhanced their death following incubation for 60 min at 43°C. Herein, the inhibitors of HSP90 activity stimulated de novo induction of additional chaperones (HSP70 and HSP27) that significantly increased the intracellular HSP levels. If the cells were treated with 17AAG or radicicol along with an inhibitor of the HSP induction (e.g. quercetin or triptolid, or NZ28), this fully prevented the increase in intracellular chaperone levels resulting from the inhibition of HSP90 activity and subsequent heating. Importantly, in the case of conjunction of all the three treatments (an inhibitor of the HSP90 activity + an inhibitor of the HSP induction + 43°C for 60 min), the reporter reactivation was retarded yet stronger while the cell death was sharply (2-3-fold) enhanced. Such an enhancement of the cytotoxicity appears to occur owing to the chaperone deficiency; when prior to heat stress both the functional activity of constitutive HSP90 and the expression of additional (inducible) chaperones are blocked in the cells.

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5. *Kostyuk S.V., Malinovskaya E.M., Ermakov A.V., Smirnova T.D., Kameneva L.V., Chvartatskaya O.V., Loseva P.A., Ershova E.S., Lyubchenko L.N., Veiko N.N.*

Cell-free DNA fragments increase transcription in human mesenchymal stem cells, activate tlr-dependent signal pathway and suppress apoptosis.

Human mesenchymal stem cells (MSCs) are now widely adopted in regenerative medicine. However, many questions on the role of different signaling pathways in the regulation of stem cell (SC) functional activity within the organism remain unanswered. In damaged regions the level of cell death increases and DNA fragments from dead cells (cell-free DNA, cfDNA) are accumulated in blood. We showed that in adipose-derived MSCs exposed in vitro to cfDNA fragments the transcription level increased (the total amount of cellular RNA and the rRNA amount rose). GC-rich CfDNA fragments (GC-DNA) activated the TLR9-dependent signal pathway: the expression of TLR9 and of TLR9-signaling pathway adapter - MyD88 - was up-regulated.

AT-rich DNA fragments did not increase the TLR9 expression, though, the MyD88 expression level rose. So we suggest that AT-DNA acts via some other receptors that nevertheless activate MyD88-dependent signalling in MSCs. We also showed that cfDNA fragments decreased the activity of caspase, an apoptotic enzyme. So, cfDNA can significantly influence the functional activity of MSC by activating TLR9- and MyD88-dependent signal pathways and lowering the apoptosis level.

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6. *Voloshchuk O.N., Marchenko M.M., Mudrak M.C.*

The change in the structural and functional organization of the guerin's carcinoma cytochrome part of respiratory chain in tumor carriers in the conditions of preliminary low-level irradiation.

The effect of low-level irradiation of tumor-bearing rats on the structural and functional organization of the cytochrome part of respiratory chain of mitochondria isolated from Guerin's carcinoma has been investigated. The maximal reduction in the mitochondrial cytochromes a, b and c content was observed at the terminal stage of Guerin's carcinoma. A low-level irradiation during initial stages of oncogenesis produced opposite changes in the mitochondrial cytochrome content. The possible mechanism of mitochondrial haem-containing cytochromes content reduction may be attributed to impairment in their formation caused by inhibition of the key enzyme of haem synthesis, 5-aminolevulinic synthase. The determined changes of the mitochondrial cytochromes quantitative content were accompanied by decreased activity of cytochrome oxidase. The preliminary low-level irradiation of the tumor-bearing animals produced further reduction in the cytochrome oxidase activity observed in all experimental periods.

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7. *Sukhova L.L., Guryeva A.V., Berezhnaya E.A., Davydov V.V.*

Activity of endogenous aldehydes catabolism enzymes in subcellular fractions of liver, heart and brain of rats at pubertal age under stress.

Activities of enzymes involved in redox transformation of endogenous aldehydes have been investigated in subcellular fractions of liver, heart, and brain of pubertal rats exposed to prolonged immobilization stress. In the liver aldo-keto reductase (AKR) activity in the postmitochondrial fraction and aldehyde dehydrogenase (ALDH) activity of the mitochondrial fraction demonstrated a more pronounced decrease in 2-month-old rats. Rat heart postmitochondrial AKR and ALDH demonstrated opposite changes in their enzymatic activities, while activity of mitochondrial ALDH remained unchanged. Brain cells create conditions that favor effective utilization of endogenous aldehydes in metabolic redox pathways.

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8. *Pisarenko O.I., Pelogeykina Yu.A., Shulzhenko V.S., Studneva I.M., Bespalova Z.D., Sidorova M.V., Azmuko A.A., Palkeeva M.E.*

The influence of inhibiting NO formation on metabolic recovery of ischemic rat heart by apelin-12.

Apelin 12 (A-12) was synthesized by the automatic solid phase method with use of Fmoc 1H-NMR spectroscopy and mass spectrometry. Effects of apelin-12 (a peptide comprised of 12 aminoacids, A-12) on recovery of energy metabolism and cardiac function were studied in isolated working rat hearts perfused with Krebs buffer (KB) containing 11 mM glucose that were subjected to global ischemia and reperfusion. A short-term infusion of $1 \mu\text{M}$ 140 A-12 in KB prior to ischemia enhanced myocardial ATP, the total adenine nucleotide pool ($\text{ATP} + \text{ADP} + \text{AMP}$) and the energy charge of cardiomyocytes ($\frac{\text{ATP} + 0.5\text{ADP}}{\text{ATP} + \text{ADP} + \text{AMP}}$) at the end of reperfusion compared with control (KB infusion) and reduced lactate content and lactate/pyruvate ratio in reperfused myocardium to the initial values. This effect was accompanied by improved recovery of coronary flow and cardiac function. Coadministration of $140 \mu\text{M}$ A-12 and $100 \mu\text{M}$ L-NAME (the nonspecific NOS inhibitor) profoundly attenuated the peptide influence on metabolic and functional recovery of reperfused hearts. The results indicate involvement of NO, formed under the peptide action, in mechanisms of cardioprotection that are tightly associated with recovery of energy metabolism in posts ischemic heart.

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9. *Baranova V.S., Rusina I.F., Guseva D.A., Prozorovskaya N.N., Ipatova O.M., Kasaikina O.T.*

The antiradical activity of plant extracts and healthful preventive combinations of these extracts with the phospholipid complex.

Using the chemiluminescence method, the effective concentration of antioxidants (AO) and its reactivity toward peroxy radicals (ARA, the k_7 constant) have been measured for 13 plant extracts. In fact all extracts demonstrated ARA higher than ionol. *Larix dahurica*, *Hypericum perforatum*, *Potentilla fruticosa*, *Aronia melanocarpa* and *Rhaponticum carthamoides* extracts showed the highest values of ARA. The combinations *Aronia* + *Raponticum* extracts; *Larix* + *Hibiscus* extracts; *Schizandra* + *Aronia* extracts were synergistic (the synergism effect \hat{I}^2 of 38%, 33% and 22%). Apparently this phenomenon is the result of the synergistic interaction between compounds present in plant extracts. The Phospholipid complex - Lipoid S40, lacking any antioxidant effect alone, showed a potent synergistic effect with *Aronia* extract ($\hat{I}^2 = 60\%$), *Silybum* extract ($\hat{I}^2 = 41\%$). Clinical trials demonstrated, that combinations $\text{Lipoid} + \text{Aronia extract}$; $\text{Lipoid} + \text{Larix extract} + \text{Hibiscus extract}$; $\text{Lipoid} + \text{Silybum extract}$; $\text{Lipoid} + \text{Q10} + \text{Rosa majalis extract}$; may be used as an additional component in the medicinal treatment, or as an individual prophylactic agent.

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10. *Lankin V.Z., Konovalova G.G., Tikhaze A.K., Nedosugova L.V.*

The influence of natural dicarbonyls on the antioxidant enzymes activity in vitro and in vivo.

Natural dicarbonyls, which may be accumulated during oxidative stress in atherosclerosis (e.g. malondialdehyde) or carbonyl stress in diabetes mellitus (glyoxal and methylglyoxal) effectively inhibited the activities of commercial preparations of antioxidant enzymes: catalase, Cu,Zn-superoxide dismutase (Cu,Zn-SOD) and Se-contained glutathione peroxidase from human and bovine erythrocytes and also rat liver glutathione-S-transferase. After incubation of human erythrocytes with 10 mM of each investigated dicarbonyls the decrease of intracellular Cu,Zn-SOD was observed. The decreased activity of erythrocyte Cu,Zn-SOD was also detected in diabetic patients with carbohydrate metabolism disturbance but effective sugar-lowered therapy was accompanied by the increase of this enzyme activity. The increase of erythrocytes activity of Cu,Zn-SOD of diabetic patients treated with metformin

(which may utilize methylglyoxal) was higher than in erythrocytase of diabetic patients subjected to traditional therapy.

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11. *Kolesov D.V., Kiselev G.A., Kudrinskiy A.A., Yaminskiy I.V.*

Study of the interaction between antigen-antibody complexes for label-free sensor application.

Nanomechanical cantilever systems have a great potential in design of the new type of label-free immunosensors. They are based on the conversion of free energy change of the surface layer of the receptor by the reaction of molecular recognition between the antigen and antibody into mechanical deformation of microcantilever. But the mechanisms of molecular interactions in the layer are still not clear.

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