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6. Gnedenko O.V., Ivanov A.S., Yablokov E.O., Usanov S.A., Mukha D.V., Sergeev G.V., Kuzikov A.V., Moskaleva N.E., Bulko T.V., Shumyantseva V.V., Archakov A.I.

Protein-protein interactions of cytochromes P450 3A4 and 3A5 with their intermediate redox partners cytochromes b5.

Molecular interactions between proteins redox partners (cytochromes Ð 450 3Ð•4, 3Ð•5 and cytochrome b5) within the monooxygenase system, which is known to be involved in drug biotransformation, were investigated. Human cytochromes Ð 450 3A4 and 3Ð•5 (CYP3A4 and CYP3A5) form complexes with various cytochromes b5: the microsomal (b5mc) and mitochondrial (b5om) forms of this protein, as well as with 2 â€œchimericâ€• proteins, b5(om-mc), b5(mc-om). Kinetic constants and equilibrium dissociation constants were determined by the SPR biosensor. Essential distinction between CYP3A4 and CYP3A5 was only observed upon their interactions with cytochrome b5om. Electroanalytical characteristics of electrodes with immobilized hemoproteins were obtained. The electrochemical analysis of CYP3A4, CYP3A5, b5mc, b5om, b5(om-mc), and b5(mc-om) immobilized on screen printed graphite electrodes modified with membranous matrix revealed that these proteins have very close reduction potentials -0.435 ï¸ -0.350 V (vs. Ag/AgCl). Cytochrome b5mc was shown to be capable of stimulating the electrocatalytic activity of CYP3A4 in the presence of its substrate testosterone.

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7. Shumyantseva V.V., Bulko T.V., Kuzikov A.V., Khan R., Archakov A.I.

Functionalization of screen printed electrodes with organic-inorganic hybrid nano-composites for bio-sensing applications.

New types of organic-inorganic hybrid nanocomposites based on nanosized Titanium (IV) oxide TiO2 (<100 nm particle size) and carbon nanotubes (CNT, outer diameter 10-15 nm, inner diamentre 2-6 nm, length 0.1-10 ï•-m) and phosphatidilcholine were elaborated for improvement of analytical characteristics of screen printed electrodes. These nanomaterials were employed as an interface for the immobilization of skeletal myoglobin. Electrochemical behavior of myoglobin on such interfaces was characterized with cyclic voltammetry (CV) and square wave voltammetry (SWV). Direct unmediated electron transfer between myoglobin and electrodes modified with organic-inorganic hybrid nanocomposites was registered. TiO2 film and CNT film are biocompartible nanomaterials for myoglobin as was demonstrated with UV-Vis spectra. The midpoint potential of Fe3+/Fe2+ pair of myoglobin corresponded to Ð•1/2 = -0,263 V for CNT film, and Ð•1/2 = -0,468 V for TiO2 nanocomposite (vs. Ag/AgCl reference electrode)

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8. Kudryashova E.V., Suhoverkov K.V., Sokolov N.N.

PEG-chitosan branched copolymers to improve the biocatalytic properties of erwinia carotovora recombinant L-asparaginase.

A new approach to the regulation of catalytic properties of medically relevant enzymes has been proposed using the novel recombinant preparation of L-asparaginase from Erwinia carotovora (EwA), a promising antitumor agent. New branched co-polymers of different composition based on chitosan modified with polyethylene glycol (PEG) molecules, designated as PEG-chitosan, have been synthesized. PEG-chitosan copolymers were further conjugated with EwA. In order to optimize the catalytic properties of asparaginase two types of conjugates differing in their architecture have been synthesized: (1) crown-type conjugates were synthesized by reductive amination reaction between the reducing end of the PEG-chitosan copolymer and enzyme amino groups; (2) multipoint-conjugates were synthesized using the reaction of multipoint amide bond formation between PEG-chitosan amino groups and carboxyl groups of the enzyme in the presence of the Woodwardâ€™s reagent. The structure and composition of these conjugates were determined by IR spectroscopy. The content of the copolymers in the conjugates was controlled by the characteristic absorption band of C-O-C bonds in the PEG structure at the frequency of 1089 cm-1. The study of catalytic characteristics of EwA preparations by conductometry showed that at physiological pH values the enzyme conjugates with PEG-chitosan with optimized structure and the optimal composition demonstrated 5-8-fold higher catalytic efficiency (kcat/Km) than the native enzyme. To certain extent, this can be attributed to favorable shift of pH-optima in result of positively charged amino-groups introduction in the vicinity of the active site. The proposed approach, chito-pegylation, is effective for regulating the catalytic and pharmacokinetic properties of asparaginase, and is promising for the development of prolonged action dosage forms for other enzyme therapeutics

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9. Spasov A.A., Chepljaeva N.I.

Potential of pharmacological modulation of level and activity incretins on diabetes mellitus type 2.

This review summarizes data on the main approaches used for the search of biologically active compounds modulating the level and physiological activity of incretins. Currently two groups of drugs are used in clinical practice: they either replenish the deficit of incretins (glucagon-like peptide-1 receptor agonists) or inhibit the degradation processes (dipeptidyl peptidase 4 inhibitors). In addition, new groups of substances are actively searched. These include non-peptide agonists of glucagon-like peptide-1 receptors, agonists/antagonists of glucose-dependent insulinotropic peptide, the hybrid polypeptides based on glucagon-like peptide-1 and glucagon

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10. Efremova A.S., Shram S.I., Drenichev M.S., Posypanova G.A., Myasoedov N.F., Mihaylov S.N.

The selective toxic effect of dialdehyde derivatives of the pyrimidine nucleosides on human tumor cells.

The impact of a number of synthetic nucleoside derivatives on the growth and survival of cultured human ovarian tumor cells (line SKOV-3) and normal human lung fibroblasts was investigated. It was shown that the dialdehyde derivatives of uridine, 1-ï•¢-D-eritrofuranozyl uracil and 3ï¸¢-O-ï•¢-D-ribofuranosyl-2ï¸¢-deoxythymidine, in contrast to their unoxidized counterparts, exert marked toxic effect on SKOV-3 cells. Cultured human fibroblasts were less susceptible to the damaging effect of the dialdehyde nucleosides. The dialdehyde derivative of 1-ï•¢-D-eritrofuranozyl uracil demonstrated greatest differences in the cytotoxic effect on these cultures: inhibition of tumor SKOV-3 cells growth on 50% or more was achieved at the concentrations of this compound ten times lower than in the case of normal fibroblasts.

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11. Petukhov V.I., Baumane L.K., Dmitriev E.V., Vanin A.F.

Nitric oxide and electrogenic metals (Ca, Na, K) in epidermal cells.
Using atomic emission spectrometry and EPR analysis metal-ligand homeostasis (MLH) has been studied in epidermal cells of 954 liquidators of the Chernobyl accident and 947 healthy individuals. A possible association of the redox status with the quantitative changes in the MLH, which could be used as discriminators of oxidative/nitrosative stress, attracts special interest. Characteristic features of oxidative stress mainly related to electrogenic metals (Ca, K, Na), were found not only among the liquidators examined, but also in some healthy individuals (18.1%); this suggests the presence of oxidative/nitrosative stress of non-radiation origin. Correlation between intracellular production of nitric oxide (NO) with quantitative changes in the electrogenic metals may indicate the possible involvement of NO in the generation of an electric potential of the cell
DOI: 10.18097/PBMC20156104503

12. Rybakova Yu.S., Kalen A.L., Eckers J.C., Fedorova T.N., Goswami P.C., Sarsour E.H.
Increased manganese superoxide dismutase and cyclin B1 expression in carnosine-induced inhibition of glioblastoma cell proliferation.
Carnosine is an endogenous dipeptide with antiproliferative properties. Here we show that carnosine selectively inhibits proliferation of human glioblastoma cells (U-118-MG) compared to breast (MB231) and oral (Cal27 and FaDu) cancer cells. Carnosine-induced inhibition of U-118-MG proliferation is associated with a significant: decrease in cellular reactive oxygen species levels, increase in manganese superoxide dismutase (MnSOD) and increase in cyclin B1 expression resulting in G2-block. We conclude that the antiproliferative property of carnosine is due to its ability to enhance MnSOD and cyclin B1 expression. These results will be of significance to the potential application of carnosine in brain cancer therapy
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13. Gorozhanskaya E.G., Sviridova S.P., Baykova V.N., Zubrikhina G.N., Dobrovolskaya M.M., Sitov A.V.
Oxidative stress in platelets at an oncopathology.
To determine the biochemical disorders in the blood coagulation mechanism associated with oxidative stress parameters of the antioxidant status were examined in platelets of 57 colorectal cancer patients, (including 21 patients before and after surgery), and 40 healthy individuals. We determined the total content of nitric oxide (NOx), levels of superoxide dismutase (Cu/ZnSOD), glutathione and malondialdehyde (MDA). Before treatment, we observed the changes in the antioxidant defense system of platelets, which did not depend on the prevalence of malignancy: elevated levels of SOD by 16% ($p<0.05$), reduced glutathione and MDA in 5.2 and 1.7 times, respectively. NOx levels did not differ from the norm. Significant shifts were found in the postoperative period: they consisted of the increase in the generation of NOx both on the third, and on the 10-th day after surgery. These changes reflect apparently platelet response to the inflammatory process associated with the surgical trauma and confirm the role of NOx as a mediator of inflammation. The content of SOD after surgery was significantly reduced, but return to a baseline on the 10-th day. Despite the significant increase in the number of platelets, no correlations of the studied parameters and their aggregation ability were found.The findings suggest that metabolic disorders in vascular-platelet hemostasis are associated with oxidative stress, which provides a basis for further study of the relationship of cancer to thrombosis
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