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In Alzheimer's disease, the regulating function of peptidyl-prolyl isomerases in particular of Pin1 associated with maintaining a balanced state of phosphorylation/dephosphorylation processes is disturbed. Taking into consideration the multifactorial impairment of the cell cycle control, this process should be considered from the standpoint of the general state of metabolic processes, and oxidative stress has one of the key positions in aging.
DOI: 10.18097/PBMC20156101057

6. Litvinova L.S., Kirienkova E.V., Mazunin I.O., Vasilenko M.A., Fattakhov N.S.

Insulin resistance pathogenesis in metabolic obesity.

In this review we discuss the molecular mechanisms of insulin resistance concomitant with metabolic inflammation. We also analyze the world results of experimental and clinical studies which aimed at identifying the molecular targets for the development of new prevention and treatment of insulin resistance.
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7. Skvortsov V.S., Alekseychuk N.N., Khudyakov D.V., Romero Reyes I.V.

pIPredict: a computer tool for predicting isoelectric points of peptides and proteins.

The data on approximate values of isoelectric point (pI) of peptides obtained during their fractionation by isoelectric focusing can be successfully used for the calculation of the pKaâ€™s scale for amino acid residues. This scale can be used for pI prediction. The data of peptide fractionation also provides information about various posttranslational modifications (PTM), so that the prediction of pI may be performed for a wide range of protein forms. In this study, pKa values were calculated using a set of 13448 peptides (including 300 peptides with PTMs significant for pI calculation). The pKa constants were calculated for N-terminal, internal and C-terminal amino acid residues separately. The comparative analysis has shown that our scale increases the accuracy of pI prediction for peptides and proteins and successfully competes with traditional scales and such methods as support vector machines and artificial neural networks. The prediction performed by this scale, can be made in our program pIPredict with GUI written in JAVA as executable jar-archive. The program is freely available for academic users at http://www.ibmc.msk.ru/LPCIT/pIPredict. The software has also the possibility of pI predicting by some other scales; it recognizes some PTM and has the ability to use a custom scale.
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8. Tananova O.N., Arianova E.A., Gmoshinskii I.V., Toropygin I.Yu., Khryapova E.V., Trusov N.V., Khotimchenko S.A., Tutel'yan V.A.

Changes in proteome profiles of rat liver microsomes induced by silicon dioxide nanoparticles.

The effect of daily intragastric administration of an aqueous dispersion of silicon nanoparticles (NPs) (the dose range from 1.0 mg/kg to 100 mg/kg body weight for 28 days) to rats on the proteomic profile of liver microsomes has been investigated by 2D-electrophoresis followed by subsequent mass spectrometry identification. The liver microsomal fraction was isolated by differential centrifugation and its protein composition was analyzed by 2D-polyacrylamide gel electrophoresis. Identification of protein spots was carried out using MALDI-TOF mass spectrometric analysis. The mass spectrometry analysis revealed the protein GRP78 (78 kD glucose-regulated protein precursor), belonging to the family of heat shock proteins. This protein present in animals of the control group was not detected in NP-treated rats of group 2 (1 mg/kg body weight/day) and group 3 (10 mg/kg body weight/day). This protein predominantly localized in the liver cell endoplasmic reticulum and plasma membrane has the chaperone biological activity. Possible mechanisms of the effects of engineered nanoparticles on biosynthetic processes in the body are discussed.
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9. Lukasheva E.V., Ribakova Yu.S., Fedorova T.N., Makletsova M.G., Arinbasarova A.Yu., Medentzev A.G., Berezov T.T.

Effect of L-lysine alpha-oxidase from Trichoderma cf. aureoviride Rifai BKMF-4268D on pheochromocytoma PC12 cell line.

L-Amino acid oxidases (L-Đ•Đ•Đž, EC 1.4.3.2) comprise a group of flavoproteins, catalyzing oxidative deamination of L-alpha amino acids to the corresponding alpha-keto acids, NH3 and Đ•2Đž2. In most cases these enzymes present homodimeric molecules with a molecular mass of 100-150 kDa, which were shown to possess antiviral, antifungal and antitumor activity. L-lysine alpha-oxidase (LO) holds an outstanding place among this group of enzymes and its biological role may differ significantly from the other L-AAO, because it cleaves an essential amino acid â€“ L-lysine without significant action on the other amino acids. Although much research has examined LO effects in the organism, the molecular basis of these effects is yet to be identified. To fill this gap, the present work addressed one of hypothetical mechanisms of LO biological action using the enzyme from Trichoderma cf. aureoviride Rifai Đ'ĐšĐœF-4268D and rat pheochromocytoma PC-12 as a model cell line. Using flow cytometry a dose-dependent cytotoxicity of LO was shown. The significant growth of intracellular reactive oxygen species levels, detected by 2,7-dichlorodihydrofluorescein assay, implies generation of peroxide as one of the molecular mechanisms of LO cytotoxic action, although this does not rule out other probable ways of LO action in the organizm.
DOI: 10.18097/PBMC20156101099

10. Plekhova N.G., Somova L.M., Drobot E.I.

The metabolism of the innate immunity cells in bacterial infections.

Metabolic activity of innate immunity cells infected by various doses of Gram-negative (Yersinia pseudotuberculosis, Salmonella enteritidis) and Gram-positive (Staphylococcus aureus, Listeria monocytogenes) bacteria has been investigated. Using various animal models we found that during the initial period (up to 2 days) changes of infection in cellular responses depend on the type of the pathogen. In response to infection caused by Gram-negative bacteria predominant neutrophil accumulation in the foci of inflammation was observed, while Gram-positive bacteria induced preferential accumulation of macrophages. The study of metabolism of these cells showed that the response of terminally differentiated primed phagocytes to pathogen appearance was higher than in cells circulating in blood. In addition to the priming state the phagocyte reactivity is influenced by the bacterial load. At a low phagocyte/microbe ratio the cells reaction is almost undetectable, while an excess of microorganisms causes (despite of the increase of the phagocytic parameters) the hyperactivation of cell metabolism and production of maximal amounts of bactericide agents, which exhibit a damaging

effect on the cell itself.
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11. Sirota T.V.

Involvement of carbonate/bicarbonate ions in the superoxide-generating reaction of adrenaline autoxidation.

An important role of carbonate/bicarbonate ions has been recognized in the superoxide generating reaction of adrenaline autooxidation in an alkaline buffer (a model of quinoid adrenaline oxidation in the body). It is suggested that these ions are directly involved not only in formation of superoxide anion radical (Ðž2 -Â·) but also other radicals derived from the carbonate/bicarbonate buffer. Using various buffers it was shown that the rate of accumulation of adrenochrome, the end product of adrenaline oxidation, and the rate of Ðž2 -Â· formation depend on concentration of carbonate/bicarbonate ions in the buffer and that these ions significantly accelerate adrenaline autooxidation thus demonstrating prooxidant properties. The detectable amount of diformazan, the product of nitro blue tetrazolium (NBT) reduction, was significantly higher than the amount of adrenochrome formed; taking into consideration the literature data on Ðž2 -Â· detection by NBT it is suggested that adrenaline autooxidation is accompanied by one-electron reduction not only of oxygen dissolved in the buffer and responsible for superoxide formation but possible carbon dioxide also dissolved in the buffer as well as carbonate/bicarbonate buffer components leading to formation of corresponding radicals. The plots of the dependence of the inhibition of adrenochrome and diformazan formation on the superoxide dismutase concentration have shown that not only superoxide radicals are formed during adrenaline autooxidation. Since carbonate/bicarbonate ions are known to be universally present in the living nature, their involvement in free radical processes proceeding in the organism is discussed.
DOI: 10.18097/PBMC20156101115

12. Kalenikova E.I., Kharitonova E.V., Gorodetskaya E.A., Tokareva O.G., Medvedev O.S.

HPLC estimation of coenzyme Q10 redox status in plasma after intravenous coenzyme Q10 administration.

The pharmacokinetics of the total pool of coenzyme Q10 (CoQ10), its oxidized (ubiquinone) and reduced (ubiquinol, CoQ10H2) forms have been investigated in rats plasma during 48 h after a single intravenous injection of a solution of solubilized CoQ10 (10 mg/kg) to rats. Plasma levels of CoQ10 were determined by HPLC with spectrophotometric and coulometric detection. In plasma samples taken during the first minutes after the CoQ10 intravenous injection, the total pool of coenzyme Q10 and proportion of CoQ10H2 remained unchanged during two weeks of storage at -20Â°C. The kinetic curve of the total pool of coenzyme Q10 corresponds to a one-part model (R2 = 0.9932), while the corresponding curve of its oxidized form fits to the two-part model. During the first minutes after the injection a significant portion of plasma ubiquinone undergoes reduction, and after 7 h the concentration of ubiquinol predominates. The decrease in the total plasma coenzyme Q10 content was accompanied by the gradual increase in plasma ubiquinol, which represented about 90% of total plasma CoQ10 by the end of the first day. The results of this study demonstrate the ability of the organism to transform high concentrations of the oxidized form of CoQ10 into the effective antioxidant (reduced) form and justify prospects of the development of parenteral dosage forms of CoQ10 for the use in the treatment of acute pathological conditions.
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13. Gylmiyarova F.N., Radomskaya V.M., Gusyakova O.A., Ryskina E.A., Kolotyeva N.A., Shahnovich E.A., Nefedova N.S., Sidorova I.F., Baisheva G.M., Pervova Yu.V., Pleten A.P.

Modeling role of pyruvate in the processes of protein-protein interaction.

Using the ABO antibody-antigen model the influence of natural metabolite pyruvate on the antibody interaction with of erythrocyte antigens, defining their group specificity has been investigated. Before agglutination reaction erythrocytes of A(II)-AB(IV) blood groups, monoclonal anti-A and anti-B antibodies were incubated with sodium pyruvate. Visualization of agglutinates was performed by means of flow cytometry and laser scanning confocal microscopy. Computer-aided prediction of the spectrum of biological activity of pyruvate by a PASS program proposed major regulatory pathways, in which pyruvate may be involved. It has been demonstrated that pyruvate can regulate the intensity of antigen-antibody interaction. These results suggest the possibility of using small molecules, for example pyruvate, as molecular probes and prospects of the use of erythrocytes with antigenic determinants of the ABO system expressed on their membranes for studies of protein-protein interactions due to convenient visualization and possibility of quantitative evaluation of this process.
DOI: 10.18097/PBMC20156101132

14. Beskaravainy P.M., Molchanov M.V., Suslikov A.V., Paskevich S.I., Kutyshenko V.P., Vorobâ€™ev S.I.

NMR study of human biological fluids for detection of pathologies.

The paper deals with the NMR spectra obtained using preparations of five different human biological body fluids. Characteristic metabolite signals of blood, urine, tears, saliva, and sweat spectra have been determined and classified. The biological body fluid samples were used for search and identification of biomarkers of cardiovascular disease. Absolute functional biomarkers for diseases such as coronary heart disease (CHD) have not been recognized even in the case acute myocardial infarction. A hypothesis explaining reasons of lack of such markers has been formulated. The results of comparative analysis of blood and urine samples from humans and some laboratory animals are given. Identify and analyze signals of metabolites of pathogenic microflora and their dynamics in the urine from patients with urogenital diseases have been determined and analyzed and characteristic biomarkers have been recognized.
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15. Glukhov A.I., Grigorieva Y.E., Gordeev S.A., Vinarov A.Z., Potoldykova N.V.

Development of noninvasive bladder cancer diagnosis on basis of telomerase and itâ€™s subunits hTERT and hTR detection.

Telomerase activity (TA) and expression of genes coding itâ€™s subunits (hTERT and hTR) have been examined in tumor tissue and urine sediment samples taken from patients with bladder cancer (BC) using the modified TRAP assay (in the case of telomerase detection) and RT-PCR (in the case of

hTERT and hTR expression). Results obtained in this study demonstrate possibility of noninvasive diagnosis of BC with sensitivity of 96% and specificity of 100% in the case of telomerase detection and with sensitivity of 80% and specificity of 100% in the case of hTERT detection in urine sediment samples.

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