Biomeditsinskaya Khimiya

ISSN 2310-6905 (online), ISSN 2310-6972 (print)

2017 volume 63 issue 2

1. Zavialova M.G., Zgoda V.G., Nikolaev E.N.

Analysis of contribution of protein phosphorylation in the development of the diseases.

In recent decades, studies in the molecular origins of socially significant diseases have made a big step forward with the development and using of high-performance methods in genomics and proteomics. Numerous studies in the framework of the global program â€œHuman Proteomeâ€• were aimed at the identification of all possible proteins in various cell cultures and tissues, including cancer. One of the objectives was to identify biomarkers - proteins with high specificity to certain pathologies. However, in many cases, it is shown that the development of the disease is not associated with the appearance of new proteins, but depends on the level of gene expression or forming of proteoforms - splice variants, single amino acid substitutions (SAP variants), and post-translational modifications (PTM) of proteins. PTM may play a key role in the development of pathology because they activate a variety of regulatory or structural proteins in the majority of cell physiological processes. Phosphorylation is among the most significant of these protein modifications.This review will describe methods for analysis of protein phosphorylation used in the studies of such diseases as cancer and neurodegenerative diseases, as well as examples of cases when the modified proteins are involved directly to their development, and screening such significant PTM is used for the diagnosis and choice of treatment.

DOI: 10.18097/PBMC20176302101

2. Maslov D.L., Balashova E.E., Lokhov P.G., Archakov A.I.

Pharmacometabonomics â€“ the novel way to personalized drug therapy.

The review is devoted to pharmacometabonomics - a new branch of science focused on personalization of drug therapy through the comprehensive analysis of metabolites of patient's biological fluids. It considers the history of pharmacometabonomic, positioning to other â€œ-omicâ€• sciences, and system approach, realized by this science, in determination of individual therapeutic dose of the drugs and also a technical implementation of pharmacometabonomic based on direct mass spectrometry of blood plasma metabolites. Special attention is paid to a comparative analysis of pharmacometabonomics and other main approaches to personalized therapy in the clinic, such as pharmacogenetics and therapeutic drug monitoring. Finally, prospects of pharmacometabonomics applications in clinical practice were also discussed.

DOI: 10.18097/PBMC20176302115

3. Grishin D.V., Pokrovskaya M.V., Podobed O.V., Gladilina Ju.A., Pokrovsky V.S., Aleksandrova S.S., Sokolov N.N.

Prediction of protein thermostability from their primary structure: the current state and development factors.

The construction of proteins and peptides with desired properties, including resistance to high temperatures, as well as optimization of their amino acid composition, is an important and complex task, which attracts much attention in various branches of the basic sciences, and also in biomedicine and biotechnology. This raises the question: what method is more relevant for the at the pilot stage of research in order to estimate the influence of the planned amino acid substitutions on the thermostability of the resultant protein construct? In this brief review we have classified existing basic practical and theoretical approaches used in studies and predicting the thermal stability of native and recombinant polypeptides. Particular attention has been paid to the predictive potential of statistical methods for studying the thermodynamic parameters of the primary protein structure and prospects of their use.

DOI: 10.18097/PBMC20176302124

4. Zhirnik A.S., Semochkina Y.P., Moskaleva E.Yu., Krylov N.I., Tubasheva I.A., Kuznetsov S.L., Vorontsov E.A.

Antineoplastic mechanisms of niclosamide-loaded nanoparticles in human colorectal cancer cells.

Using poly(lactic-co-glycolic) acid we developed a polymeric form of niclosamide (PFN) and investigated molecular mechanisms underlying its antitumor activity against human colorectal cancer cell lines (SW837, Caco-2, COLO 320 HSR). PFN was shown to be more cytotoxic against cancer cells and less cytotoxic against normal cells (human embryonic lung fibroblasts) as compared to niclosamide. Both niclosamide and its polymeric form caused mitochondrial damage (evaluated as a decrease in rhodamine 123 accumulation) and increased the levels of reactive oxygen species, particularly mitochondrial superoxide, resulting in the oxidative damage to biomolecules. Furthermore, niclosamide and PFN induced G0/G1 cell cycle arrest.

DOI: 10.18097/PBMC20176302132

5. Feoktistova E.S., Skamrov A.V., Goryunova L.E., Khaspekov G.L., Osyaeva M.K., Rodnenkov O.V., Beabealashvilli R.Sh.

Analysis of gene expression pattern in peripheral blood leukocytes during experimental heat wave.

The conditions of Moscow 2010 summer heat wave were simulated in an accommodation module. Six healthy men aged from 22 to 46 years stayed in the module for 30 days. Measurements of gene expression in peripheral blood leukocytes before, during and 3 day after simulated heat wave were performed using qRT-PCR. We observed a shift in the expression level of certain genes after heat exposure for a long time, and rapid return to the initial level, when volunteers leaved the accommodation module. Eight genes were chosen to form the â€œheat expression signatureâ€•. EGR2, EGR3 were upregulated in all six volunteers, EGR1, SIRT1, CYP51A1, MAPK9, BAG5, MNDA were upregulated in 5 volunteers.

DOI: 10.18097/PBMC20176302139

6. Kiseleva Y.Y., Ptitsyn K.G., Tikhonova O.V., Radko S.P., Kurbatov LK., Vakhrushev I.V., Zgoda V.G., Ponomarenko E.A., Lisitsa A.V., Archakov A.I.

PCR analysis of the absolute number of copies of human chromosome 18 transcripts in liver and HepG2 cells.

Using reverse transcription in conjunction with the quantitative real-time PCR or digital droplet PCR, the transcriptome profiling of human chromosome 18 has been carried out in liver hepatocytes and hepatoblastoma cells (HepG2 cell line) in terms of the absolute number of each transcript per cell. The transcript abundance varies within the range of 0.006 to 9635 and 0.011 to 4819 copies per cell for HepG2 cell line and hepatocytes, respectively. The expression profiles for genes of chromosome 18 in hepatocytes and HepG2 cells were found to significantly correlate: the Spearman's correlation coefficient was equal to 0.81. The distribution of frequency of transcripts over their abundance was bimodal for HepG2 cells and unimodal for liver hepatocytes. Bioinformatic analysis of the differential gene expression has revealed that genes of chromosome 18, overexpressed in HepG2 cells compared to hepatocytes, are associated with cell division and cell adhesion processes. It is assumed that the enhanced expression of those genes in HepG2 cells is related to the proliferation activity of cultured cells. The differences in transcriptome profiles have to be taken into account when modelling liver hepatocytes with cultured HepG2 cells.

DOI: 10.18097/PBMC20176302147

7. Tapbergenov S.O., Sovetov B.S., Tapbergenov A.T., Hahn Elina

Metabolic effects of combined introduction of adrenalin and blocker of methanoprolol beta-adrenophyleters.

The effect of combined administration of adrenaline (0.4 mg/kg, i.p.) and b1-blocker metoprolol (25 mg/kg) on the activity of glutathione peroxidase (GPO), glutathione reductase (GR), catalase, adenosine deaminase (AD), AMP deaminase (AMPD), 5Â¢-nucleotidase (5Â¢N), on the level ofmalonic dialdehyde (MDA) and conjugated dienes (CD) was investigated. In blood adrenaline administration to animals caused an increase in the activity of AMPD, AD, 5Â¢N and GPO, and the increase the level of CD in the blood increases. Metoprolol caused a more pronounced increase in the activity of blood AMPD, AD, 5'N and the amount of CD. In contrast to adrenaline, metoprolol decreased the MDA level of, and decreased the activity of GPO and catalase. Combined administration of metoprolol and adrenaline to animals was accompanied by an increase in the activity of AD, AMPD, 5Â¢N, a decrease in the activity of GR, GPO, catalase, and a decrease in MDA in the blood. In the heart, adrenaline injection was accompanied by an increase in the MDA level, a decrease in 5Â¢N activity and an increase in the ratio of the activities of the enzymes AD+AMPD/5Â¢N. Metoprolol injection reduced MDA and CD levels and the activity of GR and GPO. The combined administration of metoprolol and adrenaline in the heart was accompanied by activation of AD, AMPD and 5Â¢N, and a decrease in the amount of MDA and CD, and a decrease in the activity of GR, GPO, and catalase. In the liver adrenaline caused an increase in MDA and DC levels, activation of catalase, AD, AMPD, and 5Â¢N. Metoprolol caused a decrease in MDA and CD levels and activity of catalase and GPO, an increase in the activity of AD and AMPD in the liver. Combined administration of adrenaline and metoprolol reduced manifestations of the heart and liver oxidative stress response as compared with administration of adrenaline alone.

DOI: 10.18097/PBMC20176302154

8. Stepovaya E.A., Shakhristova E.V., Nosareva O.L., Rudikov E.V., Egorova M.Y., Egorova D.Y., Novitsky V.V.

Redox-dependent mechanisms of regulation of breast epithelial cell proliferation.

Activation of free radical oxidation in different cell types, including breast epithelial cells, may result in damage to macromolecules, in particular, proteins taking part in regulation of cell proliferation and apoptosis. The glutathione, glutaredoxin and thioredoxin systems play an essential role in maintaining intracellular redox homeostasis. Due to this fact, modulation of cellular redox status under the effect of an SH group inhibitor and an SH group protector may be used as a model for studying the role of redox proteins and glutathione in regulating cell proliferation in different pathological processes. In this study we have evaluated the state of the thioredoxin, glutaredoxin and glutathione systems as well as their role in regulating proliferation of HBL-100 breast epithelial cells under redox status modulation with N-ethylmaleimide (NEM) and 1,4-dithioerythriol (DTE). Modulating the redox status of breast epithelial cells under the effect of NEM and DTE influences the functional activity of glutathione-dependent enzymes, glutaredoxin, thioredoxin, and thioredoxin reductase through changes in the GSH and GSSG concentrations. In HBL-100 cells under redox-status modulation, we have found an increase in the number of cells in the S-phase of the cell cycle and a decrease in the number of cells in the G0/G1 and G2/Đœ phases, as opposed to the values in the intact culture. The proposed model of proliferative activity of cells under redox status modulation may be used for development of new therapeutic approaches for treatment of diseases accompanied by oxidative stress generation.

DOI: 10.18097/PBMC20176302159

9. Tamkovich S.N., Yunusova N.V., Stakheeva M.N., Somov A.K., Frolova A.Y., Kirushina N.A., Afanasyev S.G., Grigoryeva A.E., Laktionov P.P., Kondakova I.V.

Isolation and characterization of exosomes from blood plasma of breast cancer and colorectal cancer patients.

A simple approach for isolation of exosomes from the blood plasma, which allows to obtain highly purified preparations of microvesicles no larger than 100 nm has been proposed. The presence of different subpopulations of exosomes in the blood plasma of healthy donors and cancer patients has been recognized. We found the presence of the universal markers CD9, CD24 and CD81 on exosomes isolated from blood plasma that can be used to their routine typing.

DOI: 10.18097/PBMC20176302165

10. Ershov P.V., Yablokov E.O., Mezentsev Yu.V., Kalushskiy L.A., Florinskaya A.V., Veselovsky A.V., Gnedenko O.V., Gilep A.A., Usanov S.A., Medvedev A.E., Ivanov A.S.

The effect of isatin on protein-protein interactions between cytochrome b5 and cytochromes P450.

Cytochromes P450 (CYP) are involved in numerous biochemical processes including metabolism of xenobiotics, biosynthesis of cholesterol, steroid hormones etc. Since some CYP catalyze indol oxidation to isatin, we have hypothesized that isatin can regulate protein-protein interactions (PPI) between components of the CYP system thus representing a (negative?) feedback mechanism. The aim of this study was to investigate a possible effect of isatin on interaction of human CYP with cytochrome b5 (CYB5A). Using the optical biosensor test system employing surface plasmon

resonance (SPR) we have investigated interaction of immobilized CYB5A with various CYP in the absence and in the presence of isatin. The SPR-based experiments have shown that a high concentration of isatin (270 mM) increases Kd values for complexes CYB5A/CYP3Ð•5 and CYB5A/CYP3A4 (twofold and threefold, respectively), but has no influence on complex formation between CYB5A and other CYP (including indol-metabolizing CYP2C19 and CYP2E1). Isatin injection to the optical biosensor chip with the preformed molecular complex CYB5A/CYP3A4 caused a 30%-increase in its dissociation rate. Molecular docking manipulations have shown that isatin can influence interaction of CYP3Ð•5 or CYP3A4 with CYB5A acting at the contact region of CYB5A/CYP.
DOI: 10.18097/PBMC20176302170