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1. Maltsev A.V., Galzitskaya O.V.

Formation and participation of nano-amyloids in pathogenesis of Alzheimer's disease and other amyloidogenic diseases.

Studies of neurodegenetrative disorders have become particularly actual attracting the attention of researchers from over the world because of the dissemination of Alzheimer's disease. The reason for such pathogenesis is the transition of a "healthy" molecule or peptide from the native conformation into a very stable "pathological" isoform. During this, molecules in the "pathological" conformation aggregate, forming amyloid fibrils that can increase without any control. Novel knowledge is required on sporadic isoforms of Alzheimer's disease, on the nature of triggering mechanisms of conformational transitions of beta-amyloid fragments from normally functioning proteins into new formations - nano-beta-amyloids - that spiral out of control of neurons and organism which leads to the loss of neurons. Herein we review studies devoted to the formation of amyloid fibrils and their role in pathogenesis of amyloid diseases.

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2. Spiridonova V.A.

Molecular recognition elements - DNA/RNA-aptamers to proteins.

In this review summarizes data on DNA/RNA aptamers - a novel class of molecular recognition elements. Special attention is paid to the aptamers to proteins involved into pathogenesis of wide spread human diseases. These include aptamers to serine protease, to cytokines/growth factors, to influenza viral protein, nucleic acid binding proteins. Strong and specific binding for a given protein target of aptamers make them an attractive class of direct protein inhibitors. They can inhibit pathogenic proteins and it is becoming clear that aptamers have the potential to be a new and effective class of therapeutic molecules.

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3. Kulinsky V.I., Kolesnichenko L.S.

Nuclear glutathione and its functions.

During recent years the nuclear localization of glutathione has been confirmed and this fraction has been quantitatively determined. The nuclear GSH and the enzymes of its metabolism realize independent and important functions. They considerably differ from functions of hyaloplasmic and mitochondrial GSH. Glutathione interacts with regulatory pathways, involved into signal transmission into the nucleus.

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4. Ki Beom Lee , Kyung Bae Pi

Comparative proteomic analysis of cancerous and adjacent normal lung tissues.

Lung cancer is the leading cause of cancer-related mortality in industrialized countries. Unfortunately, most lung cancers are found too late for a cure, therefore early detection and treatment is very important. We have applied proteomic analysis by using two-dimensional gel electrophoresis and peptide mass fingerprinting techniques for examination of cancerous and adjacent non-cancerous lung tissues from the same patient. The aim of the study was to find proteins, which could be used as biomarkers for diagnosis and monitoring of this disease. Indeed, we found differences in expression of several proteins, related to various cellular activities, such as, chaperoning (e,g. GRP96, GRP78, HSP27), metabolism and oxidation stress (e.g. L-fucose, GST), cytoskeleton (e.g., tubulin beta 2/3, beta actin), cell adhesion (e.g. annexin A5/3), binding proteins (e.g. 14-3-3 theta) and signal transduction. These changes may be important for progression of carcinogenesis; they may be used as the molecular-support for future diagnostic markers.

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5. Tsoy A.M., Zaytseva-Zotova D.S., Edelweiss E.F., Bartkowiak A., Goergen J-L., Vodovozova E.L., Markvicheva E.A.

Microencapsulated multicellular tumor spheroids:preparation and use as a novel in vitro model for drug screening.

In the current study a technique for microencapsulation of human breast adenocarcinoma cells MCF-7 in alginate-chitosan microcapsules is used. Microencapsulation is proposed to generate multicellular tumor spheroids (MTS) based on these cells and to test them further as an in vitro model for anti-tumor drug screening. Cytotoxicity of methotrexate (MTX) was studied on the obtained MTS. A set of MTS with mean size of 150, 200 and 300 m was prepared in function of a cultivation time. After incubation of MTS in cultivation medium containing MTX at concentrations of 1, 2, 10, 50 and 100 nM for 48 hs cell viability was evaluated. MTS were shown to be more resistant to MTX than the monolayer culture, and the resistance to MTX was increased with enhancing a spheroid size. At MTX concentration of 100 nM a number of viable cells in MTS with the size of 300 m was 2.5-fold bigger than that one in monolayer culture. It is suggested that the cells in microencapsulated MTS can better mimic cell behavior in a small size solid tumor than the cells in a monolayer culture. In future microencapsulated MTS can be proposed as a novel in vitro model for anticancer drug screening.

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6. Veiko N.N., Konorova I.L., Neverova M.E., Fidelina O.V., Mkrtumova N.A., Ershova E.S., Postnov A.Iu., Kon'kova M.S.

Delayed appearance of hypertension in spontaneously hypertensive rat (SHR) injected with CpG-rich DNA early in ontogenesis.

In this study we have investigated properties of blood serum extracellular DNA (cell-free DNA) from patients with essential arterial hypertension (AH). Cell-free DNA concentration was not changed in the control AH group compared to norma (healthy donors) but fragments of CpG-rich cell-free DNA marker content were increased at transcribed area of ribosomal repeat (TArDNA, CpG-DNA). To evaluate effect of CpG-DNA on AH development in 2-day SHR line and in control normotensive line (WKY), 700 ng of human TArDNA single subcutaneous injection were inoculated to obtain anti-CpG-DNA polyclonal antibodies. These antibodies could change CpG-DNA contents in total cell-free DNA. Blood pressure (BP) in 9-week SHR line rats immunized with CpG-DNA was equal to BP of WKY rats. Then BP of immunized SHR steadily increased with age and reached high value 8 weeks later compared to control SHR rats. Cell-free DNA analysis in 17-week SHR line rats showed significantly reduced concentrations of cell-free DNA and also showed decrease in small DNA fragments content, but increased content of CpG-DNA (rat TArDNA). These changes were accompanied with 3.5-fold blood endonuclease activity increase and decrease of free (unbound to cell-free DNA) anti-CpG-DNA antibodies quantity. Total anti-CpG-DNA antibodies quantity in immunized rats wasn't changed compared to control animals. Thus, observed effect of increase in stable BP elevation age in immunized SHR line rats doesn't relate to increase of anti-CpG-DNA antibody production. Possible reason of this effect is further discussed.
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7. Shpakov A.O., Derkach K.V., Bondareva V.M.

A decrease of sensitivity of adenylyl cyclase and heterotrimeric g-proteins to chorionic gonadotropin and peptide hormones action in the tissues of reproductive system of the rats in the condition of experimental type 2 diabetes.

Patients with different forms of the diabetes, particularly with insulin-independent type 2 diabetes have a wide spectrum of the disturbances of the functions of reproductive system. It is supposed that the main reason of these disturbances is altered sensitivity of reproductive system tissues to regulatory action of hormones. The aim of the work was the identification of the changes in functioning of human chorionic gonadotropin (hCG) - and peptide hormones-sensitive adenylyl cyclase system (ACS) in the ovary, testes and uterus of rats with neonatal streptozotocin (STZ) diabetes that is similar to the type 2 diabetes in humans. The effects of hCG, PACAP-38 and relaxin, realizing their effects via G-protein of the stimulatory type (Gs), and somatostatin, acting via G-protein of the inhibitory type (Gi), on adenylyl cyclase (AC) activity and the GTP binding of the G-proteins were studied. Regulatory effects of hCG and PACAP-38 decreased in the ovary and testes of rats with STZ type 2 diabetes, while the effects of somatostatin decreased in all investigated tissues (in a considerable extent in the uterus). This expressed in the weakening of hormonal effects on AC activity, stimulating in the case of hCG and PACAP-38 and inhibiting in the case of somatostatin, and in the decrease of stimulation of the GTP binding by the hormones. At the same time a significant decrease of ACS sensitivity to relaxin in the tissues of diabetic rats was not found. Data obtained suggest that the key reason of the disturbances of reproductive functions in experimental type 2 diabetes is the decrease of ACS sensitivity to the hormones, such as hCG, PACAP-38 and somatostatin, that play a important role in functioning of reproductive system.
DOI: 10.18097/PBMC20105606700

8. Dremza I.K., Cheshchevik V.T., Zabrodskaya S.V., Maksimchik Y.Z., Sudnikovich E.Ju., Lapshina E.A., Zavodnik I.B.

Hepatotoxic efects of acetaminophen. Protective properties of tryptophan-derivatives.

Rat intoxication with acetaminophen (APAP) (500-1500 mg/kg body weight intragastrically) caused a considerable dose-dependent decrease in reduced glutathione (GSH) level in both liver cellular cytoplasm and mitochondria (at the dose 1500 mg/kg body weight by 60% and 33%, respectively). The cytoplasmic GSH level decreased more pronounced by comparison with that in mitochondria. At the same time, we did not observe any inactivation of the mitochondrial enzymes: succinate dehydrogenase, Î±-ketoglutarate dehydrogenase, glutathione peroxidase despite of mitochondrial GSH consumption; also we did not observe any decrease in the respiratory activity of liver mitochondria isolated from APAP-intoxicated rats. A tryptophan derivative, melatonin (10 mg/kg body weight), did not prevent intramitochondrial GSH oxidation, but decreased the hepatoxity of APAP, diminishing the activities of AlT and AsT as well as bilirubin level in blood plasma of intoxicated rats. N-acetyl-nitrosotryptophan (a nitric oxide donor) did not exhibit any hepatoprotective effects.
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9. Blagonravov M.L., Onufriev M.V., Demurov E.A., Guliaeva N.V., Frolov V.A.

Assessment of caspase-3 activity in rabbit myocardial tissue during experimental hemodynamic overload of the left ventricle of the heart.

It's well known that chronic overload of the cardiac left ventricle is accompanied by an increase in the cardiomyocyte apoptosis rate. However direction and extent of programmed cell death changes under an acute overload of the left ventricle still requires detailed investigation. Caspase-3 activity has been investigated in myocardium of rabbits on the 1, 3 and 5 days after modeling of left ventricle hemodynamic overload caused by surgical narrrowing of the ascending aorta. Control group included intact animals. It was found that caspase-3 activity significantly increased in both ventricles on day 1; it increased more than twofold above controls on day 3; it began to decrease by day 5. On the basis of the obtained data it was concluded that: an acute hemodynamic overload of the left ventricle is a cause of apoptosis acceleration in the myocardial tissue of both cardiac ventricles during first days of the investigated process.
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10. Pozdeev V.K., Pozdeyev N.V.

Determination of total aminothiols and neuroactive amino acids in plasma by high performance liquid chromatography with fluorescence detection.

This paper describes a simple and sensitive reversed-phase HPLC method for the determination of total homocysteine, total cysteine, total glutathione (GSH+GSSG), and neuroactive amino acids (Asp, Glu, Tau, GABA) using precolumn derivatization with ortho-phtaldialdehyde and fluorimetric detection at 360 and 470 nm for emission and excitation, respectively. Derivatization was performed with ortho-phthaldialdehyde in the presence of 2-mercaptoethanol after alkylation of the free sulfhydryl groups with iodoacetic acid. For determination of total aminothiols, the disulfide bonds were reduced and protein-bound thiols were released by addition of dithiothreitol to the plasma sample. The advantage of this method is the simultaneous

determination of both homocysteine/cysteine/glutathione and neuroactive amino acids in the sample. The plasma levels of studied compounds were determined in 14 healthy volunteers (20-45 years old) and 55 patients with chronic hepatitis C (20-49 years old) and the resulting numbers were in a good agreement the studies published earlier. The calibration curves were linear over a concentration range of 5-100 Î¼M in plasma (r2=0.985-0.996). The intraday and interday coefficients of variation were 3-6% and 4-7%, respectively. The recovery of the standards added to the plasma samples ranged from 94 to 102%. The limits of detection (LOD) were 0.2-0.5 ng per 10 Î¼l injection volume (signal-to-noise ratio of 3).
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11. Levashov P.A., Afanasieva O.I., Dmitrieva O.A., Klesareva E.V., Adamova I.Yu., Afanasieva M.I., Bespalova Zh.D., Sidorova M.V., Pokrovsky S.N.
Preparation of affinity sorbents with immobilized synthetic ligands for therapeutic apheresis.
Preparation and stability of a few examples of medical sorbents are described. A simple and practical technique has been developed for sorbent preparation with the low weight synthetic ligands such as amino acids, peptides or oligosaccharides. This approach to sorbent preparation enables the development of the new affine columns generation for medicine and biotechnology to be carried out with ease.
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12. Korzhenevskiy D.A., Selischeva A.A., Saveliev S.V.
An approach to the identification of the phospholipid molecular species in human erythrocytes using HPLC with mass-spectrometric detection.
A modified RP-HPLC-MS approach has been proposed for a single run separation and identification of the molecular species of different phospholipid classes in a complex extract. This approach has been applied to the analysis of glycero- and sphingolipid composition of human erythrocytes and a number of ceramide fractions have been identified; these fractions was missed in previous studies employing similar methods. The fine experimental design leads to the decrease in the number of procedures needed for a complete phospholipid profiling of the sample.
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13. Shumyantseva V.V., Bulko T.V., Vagin M.Yu., Suprun E.V., Archakov A.I.
Electrochemical immunoanalysis of cardiac myoglobin.
Method targeting the direct monitoring of myoglobin based on analysis of electrochemical parameters of modified electrodes were proposed. Method of direct detection is based on interaction of myoglobin with anti-myoglobin with subsequent electrochemical registration of hemeprotien. Myocardial infarction biomarker myoglobin was quantified at biological level using screen printed electrodes modified with gold nanoparticles stabilized with didodecyldimethylammonium bromide (DDAB) and antibodies. Proposed method did not require signal enhancement and amplification and also labeled secondary antibodies. Electro analysis has high specificity and sensitivity. Myoglobin -antibodies interaction was studied also with electrochemical impedance spectroscopy. Sensor has low detection limit and broad diapason of working concentrations (17.8 ng/ml - 1780 ng/ml; 1 nM - 10 nM). Method based on gold nanoparticles detection on the surface of electrodes was treated for myoglobin identification. AuNP worked as an electrochemical sensing platform: the oxidation of gold surface (resulted in gold oxide formation) upon polarization served as a basis for analytical response. The difference of cathodic peak area and peak high of gold oxide reduction in the case of electrodes with antibodies and electrodes with antibodies - myoglobin complex, was registered.
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