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1. Poteryaeva O.N., Usynin I.F.

Antidiabetic role of high density lipoproteins.

Disturbance in lipid metabolism can be both a cause and a consequence of the development of diabetes mellitus (DM). One of the most informative indicator of lipid metabolism is the ratio of atherogenic and antiatherogenic fractions of lipoproteins and their protein components. The review summarizes literature data and own results indicating the important role of high-density lipoprotein (HDL) and their main protein component, apolipoprotein A-I (apoA-I), in the pathogenesis of type 2 DM. On the one hand, HDL are involved in the regulation of insulin secretion by b-cells and insulin-independent absorption of glucose. On the other hand, insulin resistance and hyperglycemia lead to a decrease in HDL levels and cause modification of their protein component. In addition, HDL, possessing anti-inflammatory and mitogenic properties, provide anti-diabetic protection through systemic mechanisms. Thus, maintaining a high concentration of HDL and apoA-I in blood plasma and preventing their modification are important issues in the context of prevention and treatment of diabetes.

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2. Kugaevskaya E.V., Gureeva T.A., Timoshenko O.S., Solovyeva N.I.

The urokinase-type plasminogen activator system and its role in tumor progression.

In the multistage process of carcinogenesis, the key link in the growth and progression of the tumor is the invasion of malignant cells into normal tissue and their distribution and the degree of destruction of tissues. The most important role in the development of these processes is played by the system of urokinase-type plasminogen activator (uPA system), which consists of several components: serine proteinase â€“ uPA, its receptor â€“ uPAR and its two endogenous inhibitors â€“ PAI-1 and PAI-2. The components of the uPA system are expressed by cancer cells to a greater extent than normal tissue cells. uPA converts plasminogen into broad spectrum, polyfunctional protease plasmin, which, in addition to the regulation of fibrinolysis, can hydrolyze a number of components of the connective tissue matrix (Ð¡TM), as well as activate the zymogens of secreted matrix metalloproteinases (MMÐ) â€“ pro-MMÐ . MMÐ s together can hydrolyze all the main components of the Ð¡TM, and thus play a key role in the development of invasive processes, as well as to perform regulatory functions by activating and releasing from STM a number of biologically active molecules that are involved in the regulation of the main processes of carcinogenesis. The uPA system promotes tumor progression not only through the proteolytic cascade, but also through uPAR, PAI-1 and PAI-2, which are involved in both the regulation of uPA/uPAR activity and are involved in proliferation, apoptosis, chemotaxis, adhesion, migration and activation of epithelial-mesenchymal transition pathways. All of the above processes are aimed at regulating invasion, metastasis and angiogenesis. The components of the uPA system are used as prognostic and diagnostic markers of many cancers, as well as serve as targets for anticancer therapy.

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3. Alessenko A.V., Lebedev A.T., Kurochkin I.N.

The role of sphingolipids in cardiovascular pathologies.

Cardiovascular diseases (CVD) remain the leading cause of death in industrialized countries. One of the most significant risk factors for atherosclerosis is hypercholesterolemia. Its diagnostics is based on routine lipid profile analysis, including the determination of total cholesterol, low and high density lipoprotein cholesterol, and triglycerides. However in recent years, much attention has been paid to the crosstalk between the metabolic pathways of the cholesterol and sphingolipids biosynthesis. Sphingolipids are a group of lipids, containing a molecule of aliphatic alcohol sphingosine. These include sphingomyelins, cerebrosides, gangliosides and ceramides, sphingosines, and sphingosine-1-phosphate (S-1-P). It has been found that catabolism of sphingolipids is associated with catabolism of cholesterol. However, the exact mechanism of this interaction is still unknown. Particular attention as CVD inducer attracts ceramide (Cer). Lipoprotein aggregates isolated from atherosclerotic pluques are enriched with Cer. The level of Cer and sphingosine increases after ischemia reperfusion of the heart, in the infarction zone and in the blood, and also in hypertension. S-1-P exhibits pronounced cardioprotective properties. Its content sharply decreases with ischemia and myocardial infarction. S-1-P presents predominantly in HDL, and influences their multiple functions. Increased levels of Cer and sphingosine and decreased levels of S-1-P formed in the course of coronary heart disease can be an important factor in the development of atherosclerosis. It is proposed to use determination of sphingolipids in blood plasma as markers for early diagnosis of cardiac ischemia and for hypertension in humans. There are intensive studies aimed at correction of metabolism S-1-P. The most successful drugs are those that use S-1-P receptors as a targets, since all of its actions are receptor-mediated.

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4. Liao P.-C., Zgoda V.G., Novikova S.E., Farafonova T.E., Tikhonova O.V., Shushkova N.A., Vavilov N.E.

Quantitative proteomics of human blood exosomes.

Exosomes are extracellular membrane vesicles secreted by cells into biological fluids. The outer membrane of exosomes protects their content from degradation and contains markers of the parent cell. Almost all cells of the body produce exosomes, however, tumor cells secrete them more intensively. Due to fact that exosomes contain proteins of cells secreting them, these vesicles could be a valuable source for biomarkers discovery. Currently, a number of studies prove the participation of exosomes in carcinogenesis. However, there is a problem of isolating pure and characterized exosomes for further use in investigation of functions or identification of tumor protein biomarkers. In this work, we have performed experiments on

exosomes isolation from human plasma by three methods: differential ultracentrifugation, ultracentrifugation in sucrose cushion, sedimentation of the exosomal fraction from serum by using a commercial kit. The protein composition of the obtained samples was determined by mass spectrometric methods of selected reactions monitoring (SRM) and shotgun proteomic analysis. The obtained exosomal samples were searched for the presence of exosomal markers (CD9, CD82, HSPA8, CD63). In the samples of exosomes isolated by ultracentrifugation with the sucrose cushion, the content of the above markers was determined as 32.85, 15.59, 6.07 fmol/mg of total protein, correspondently. It was shown that the centrifugation method with the sucrose cushion was optimal for the isolation of exosomes.
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5. Sanzhakov M.A., Prozorovskiy V.N., Ipatova O.M., Torkhovskaya T.I., Tikhonova E.G., Medvedeva N.V., Zakharova T.S.

Increase of antituberculosis efficiency of rifampicin embedded into phospholipid nanoparticles with sodium oleate.

The formulation of the antituberculosis drug rifampicin embedded into 20-30 nm nanoparticles from soy phosphatidylcholine and sodium oleate, is characterized by greater bioavailability as compared with free drug substance. In this study higher antituberculosis activity of this formulation was shown. Rifampicin in nanoparticles demonstrated more effective inhibition of M. tuberculosis H37Rv growth: minimal inhibiting concentration (MIC) was twice smaller than for free rifampicin. Administration of this preparation to mice with tuberculosis induced by M. tuberculosis Erdman revealed that after 6 weeks of oral administration the CUF value in lung was 22 times smaller for rifampicin in nanoparticles than for free drug (1.7 un. vs. 37.4 un.). The LD50 value in mice was two fold higher for rifampicin in nanoformulation.
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6. Kuritcyna N.A., Bychkov E.R., Shabanov P.D., Karpova I.V., Mikheev V.V., Marysheva V.V.

Central monoaminergic systems sensitivity to acute hypoxia with hypercapnia changes after the maintenance under the long-term social isolation.

The experiments were performed in male albino outbred mice kept in a group and under the conditions of long-term social isolation. The changes in the monoaminergic systems of the left and right hemispheres of the brain after acute hypoxia with hypercapnia have been studied. The levels of dopamine (DA), serotonin (5-HT) and their metabolites â€“ dioxyphenylacetic (DOPAC), homovanillic (HVA), and 5-hydroxyindoleacetic (5-HIAA) acids â€“ were determined by HPLC in the cerebral cortex, hippocampus and striatum of the right and left sides of the brain. In the control mice kept both in the group and under the conditions of social isolation, a higher content of DA in the cortex of the left hemisphere has been found. In the other brain structures the monoamine content was symmetric. In the cerebral cortex of the mice in the group, acute hypoxia with hypercapnia led to a right-sided increase in the DA and 5HT levels. At the same time, the DOPAC content decreased in the left cortex. In mice in the group, under the hypoxia with hypercapnia conditions, the DA level in the left hippocampus increased. In the striatum, the content of monoamines and their metabolites did not change significantly. In animals kept for a long time under the conditions of social isolation, hypoxia with hypercapnia no statistically significant changes in the monoamines and their metabolites levels were found. It has been concluded that the preliminary maintenance under the conditions of prolonged social isolation changes the reaction of central monoaminergic systems to acute hypoxia with hypercapnia.
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7. Kanygina A.V., Sharova E.I., Sultanov R.I., Schelygin Y.A., Doludin Y.V., Kostryukova E.S., Generozov E.V.

Targeted gene sequencing panels: applicability for neoantigen profiling of colon and rectal adenocarcinoma.

Cancer immunotherapy represents a promising and rapidly developing approach for the treatment of oncological diseases. Among the methods of personalized adjuvant immunotherapy, neoantigenic peptide-based drugs have demonstrated substantial efficiency. These drugs are designed to target mutant proteins arising from somatic alterations in the genome of tumor cells and thus stimulate immune response against tumor tissues. The methods of individual screening for potentially immunogenic mutations are mostly based on next-generation exome sequencing of tumor samples, which is a complex and costly procedure for clinical application. Targeted gene sequencing panels limited to a certain set of genes represent a reasonable alternative to WES. Targeted sequencing is also more efficient when there is a low amount of the sample DNA available. We have estimated the potential efficiency of targeted oncological panels in terms of somatic neoantigen profiling in colorectal cancer (colon and rectal adenocarcinoma). The clinical practice of identification of frequent somatic variants does not provide enough data for designing an efficient personalized drug when applied to low and medium mutated cancers such as colorectal cancer. Our analysis of 11 commercially available panels containing different number of genes has shown that neither the larger size of a panel nor its initial customization for colorectal cancer provides a significantly better estimation of an individual somatic mutation profile. The optimal approach is to use the general-purpose medium-sized cancer panels (2300-11200 amplicons and/or 150-600 genes). These panels allow to detect a sufficient number of immunogenic epitopes (>3) per patient for over 30-50% of patients.
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8. Luneva S.N., Nakoskina N.V., Borzunov D.Yu., Mokhovikov D.S., Vykhovanets E.P.

Concentration of several osteotropic growth factors, markers of osteogenesis and biologically active molecules in the blood serum of patients with congenital pseudarthrosis of tibia during orthopaedic treatment with combined technologies.

Congenital pseudarthrosis of tibia is a genetic, systemic pathology with impaired bone remodeling and unknown pathogenetic mechanisms. Orthopaedic treatment of the disease can fail in some cases. The process of bone remodeling is known to occur under control of local and systemic growth factors, and we sought to explore several osteotropic growth factors, markers of osteogenesis and biologically active molecules in the blood serum of patients with congenital pseudarthrosis of tibia. The study included 12 patients with congenital pseudarthrosis of tibia and anatomical shortening of 2.5Â±1.1 cm. The' age of patients ranged from 7 years to 18 years. Blood serum was used for enzyme immunoassay analysis. The own blood serum levels of 103 conditionally healthy individuals (of mean age of 13.0Â±0.27 years) were considered as the norm. Greater changes in the concentration were detected among vascular endothelial and transforming growth factors. The patients showed imbalance in serum TGF, low reparative potential of bone tissue due to osteoclast activation prevailing over differentiation of osteoblasts, progenitor and mesenchymal cells. Dynamics in

serum concentration of IGF at the time of frame removal indicated to terminating osteoblast activation and collagen synthesis and concomitant active bone restructuring.
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