

1. Kit O.I., Vodolazhsky D.I., Rostorguev E.E., Porksheyan D.H., Panina S.B.

The role of micro-RNA in the regulation of signal pathways in gliomas.

Gliomas are invasive brain tumors with high rates of recurrence and mortality. Glioblastoma multiforme (GBM) is the most deadly form of glioma with nearly 100% rate of recurrence and unfavorable prognosis in patients. Micro-RNAs (miR) are the class of wide-spread short non-coding RNAs that inhibit translation via binding to the mRNA of target genes. The aim of the present review is to analyze recent studies and experimental results concerning aberrant expression profiles of miR, which target components of the signaling pathways Hedgehog, Notch, Wnt, EGFR, TGF β , HIF1 α in glioma/glioblastoma. Particularly, the interactions of miR with targets of 2-hydroxyglutarate (the product of mutant isocytate dehydrogenase, R132H IDH1, which is specific for the glioma pathogenesis) have been considered in the present review. Detecting specific miRNAs in tissue and serum may serve as a diagnostic and prognostic tool for glioma, as well as for predicting treatment response of an individual patient, and potentially serving as a mechanism for creating personalized treatment strategies

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2. Grigorenko V.G., Rubtsova M.Yu., Uporov I.V., Ishtubaev I.V., Andreeva I.P., Shcherbinin D.S., Veselovsky A.V., Egorov A.M.

Bacterial TEM-type serine beta-lactamases: structure and analysis of mutations.

Beta-lactamases (EC 3.5.2.6) represent a superfamily containing more than 2,000 members: it includes genetically and functionally different bacterial enzymes capable to destroy the beta-lactam antibiotics. The most common are beta-lactamases of molecular class A with serine in the active center. Among them, TEM-type beta-lactamases are of particular interest from the viewpoint of studying the mechanisms of the evolution of resistance due to their broad polymorphism. To date, more than 200 sequences of TEM-type beta-lactamases have been described and more than 60 structures of different mutant forms have been presented in Protein Data Bank. We have considered the main structural features of the enzymes of this type with particular attention to the analysis of key drug resistance and the secondary mutations, their location relative to the active center and the surface of the protein globule. We have developed the BlaSIDB database (www.blasidb.org) which is an open information resource combining available data on 3D structures, amino acid sequences and nomenclature of the corresponding forms of beta-lactamases.

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3. Starikova E.V., Prianichnikov N.A., Zdobnov E., Govorun V.M.

Bioinformatics analysis of antimicrobial resistance genes and prophages colocalized in human gut metagenomes.

The constant increase of antibiotic-resistant strains of bacteria is caused by extensive uses of antibiotics in medicine and animal breeding. It was suggested that the gut microbiota serves as a reservoir for antibiotics resistance genes that can be carried from symbiotic bacteria to pathogenic ones, in particular, as a result of transduction. In the current study, we have searched for antibiotics resistance genes that are located inside prophages in human gut microbiota using PHASTER prophage predicting tool and CARD antibiotics resistance database. After analysing metagenomic assemblies of eight samples of antibiotic treated patients, *IsaE*, *mdfA* and *cpxR/cpxA* genes were identified inside prophages. The abovementioned genes confer resistance to antimicrobial peptides, pleuromutilin, lincomycins, streptogramins and multidrug resistance. Three (0.46%) of 659 putative prophages predicted in metagenomic assemblies contained antibiotics resistance genes in their sequences.

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4. Timoshenko O.S., Gureeva T.A., Kugaevskaya E.V., Zavalishina L.E., Solovyeva N.I.

Interstitial collagenase and their endogenous regulators in squamous cell cervical carcinoma.

Interstitial collagenase (MMP-1) belongs to the family of matrix metalloproteinases (MMP), which play a key role in generalization processes of invasion and metastasis, which determine the degree of tumor malignancy. MMP-1 refers to secreted, inducible MMP, the expression of which in normal tissues is not defined. Induction of expression of MMP in CSS in the tumor occurs under the action of oncogenes of HPV, and in areas adjacent to the tumor normal tissue under the action of the inductor expression of MMP "EMMPRIN (CD147), which expressively on the surface of tumor cells. The aim of this study is to determine the possibility of expression of MMP-1 and its regulators (tissue inhibitors TIMP-1 and activator - plasminogen activator "ADF) in morphologically normal body of the uterus during CSS. The study was carried out using on a tissue "postoperative specimens of the uterus when the diagnosis of CSS. All of the samples was expressed HPV16 gene E7. It was shown that: 1. The increase of MMP-1 expression, low expression (or lack thereof) of its inhibitors TIMP-1 and a very clear expression of the activator take place in the tumor when CSS that lead to increased activity of MMP-1, and aims to increase the destructive (invasive) potential of the tumor. 2. In morphologically normal tissue of the uterus during CSS the expression of MMP-1 can occur from the vaginal wall to the bottom of the uterine cavity, but at a much lower level than in the tumor. 3. These data indicate the possibility of development of a destructive process in morphologically normal body tissues of the uterus during CSS, important for understanding the mechanism of tumor progression, and suggest participation in the process of expression of MMP-1 signaling by the type of epithelial-mesenchymal interaction.

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5. Zinchuk V.V., Firago M.E.

Participation of melatonin in regulation of blood oxygen-transport function in oxidative stress induced by injection of lipopolysaccharide.

The contribution of melatonin to the regulation of the blood oxygen transport function was studied during oxidative stress induced by a triple injection of lipopolysaccharide (at a dose of 5 mg/kg) in conditions of erythropoietin and gasotransmitters (nitrogen monoxide, hydrogen sulfide) action. In the experimental groups, intraperitoneal injections of melatonin (5 mg/kg), erythropoietin (1000 U/kg), hydrogen sulfide donor (NaHS 5 mg/kg), and L-arginine (100 mg/kg), were performed. The use of melatonin alone or in combination with erythropoietin, sodium hydrosulfide or L-arginine led to a decrease in lipid peroxidation products and an increase in the antioxidant protection. Melatonin, during lipopolysaccharide administration, caused changes of blood oxygen transport function: blood oxygen saturation increased, hemoglobin oxygen affinity increased. The modifying effect of melatonin on the blood oxygen transport function in combination with erythropoietin and gasotransmitters did not exceed the effect of melatonin alone.

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6. *Konoplja A.I., Litvinova E.S., Sunyaykina O.A., Bushmina O.N., Harchenko A.V., Konoplja A.A.*

Disorders in structural-functional properties of erythrocytes in experimental acute destructive pancreatitis of alcohol etiology and their correction.

The effects of various combinations of pharmacological agents on parameters characterizing red blood cell (RBC) membrane proteins and lipids have been investigated in RBC isolated from Wistar male rats with acute destructive pancreatitis induced under conditions of forced alcoholization for 60 days. Administration of a combination of Hepon, Hypoxenum, and Phosphogliv normalized 22.5% of parameters altered change during development of acute destructive pancreatitis under conditions of chronic alcoholization of parameters, corrected towards normal values 42.5% of parameters (35% of parameters remained unchanged). Administration of Glutoxim, Mexidol and Heptral, was more effective: this combination normalized 50.0% of parameters studied, corrected towards normal values 37.5% of parameters, leaving unchanged only 12.5% of parameters studied.

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7. *Skuratovskaia D.A., Sofronova J.K., Zatolokin P.A., Vasilenko M.A., Litvinova L.S., Mazunin I.O.*

The association of the mitochondrial DNA oriB variants with metabolic syndrome.

Different genes are involved in the development of pathology and formation the metabolic syndrome (MS) phenotype. In the literature, there is a data connection to the site oriB polymorphisms of mitochondrial DNA (mtDNA), known as 16184-16193 polycytosine tract, with insulin resistance, type 2 diabetes (T2DM) and other metabolic abnormalities in different ethnic populations. It is supposed that for certain polymorphisms at this site decreases mtDNA copy number in the cells. In this study, we have identified different allelic variants of the mtDNA oriB site in MS patients (n=106) and healthy individuals (n=71) using capillary sequencing, and determined the amount of mtDNA copy blood leukocytes by droplet digital polymerase chain reaction (ddPCR). The continuous polycytosine tract was significantly more common in MS patients, and such a link was particularly strong in MS patients with type 2 diabetes (p<0.01). No significant correlation has been found between mtDNA copy number and the oriB site variants, but in general there is a tendency to decreased mtDNA copy number in MS patients.

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8. *Rayev M.B., Zamorina S.A., Litvinova L.S., Yurova K.A., Khaziakhmatova O.G., Timganova V.P., Bochkova M.S., Kropaneva M.D., Khramtsov P.V.*

The influence of chorionic gonadotropin on phenotype conversion and hTERT gene expression by T-lymphocytes of different degrees of differentiation.

The effects of chorionic gonadotropin (hCG) on the expression of the hTERT gene in combination with the conversion of the phenotype of naive T-cells and T-cells of immune memory in vitro were studied. hCG inhibited expression of hTERT mRNA in naive T-cells (CD45RA+) and immune memory T cells (CD45RO+), causing a decrease in the replicative potential of the cells. The presence of hCG in the culture led to the conversion of the phenotype of T-lymphocytes. hCG reduced the number of proliferating T-cells of immune memory, estimated by phenotypic signs by differential gating. hCG (10 IU/ml and 100 IU/ml) inhibited expression of CD25 by the studied populations, but did not modulate expression of the CD71 proliferation marker. Thus, hCG inhibited the functional activity of naive T-cells and T-cells of immune memory, which, in the context of pregnancy, can contribute to the formation of immune tolerance to the semi-allogenic fetus.

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9. *Myasoedov N.F., Lyapina L.A., Andreeva L.A., Obergan T.Yu., Grigoryeva M.E., Shubina T.A.*

Oxoprolinic short peptides – potential pharmacological means of hypolipidemic and antithrombotic actions.

One of the most urgent and important tasks of modern biological and medical research is the search and research of pharmacological agents that combine lipid-lowering and antithrombotic effects in the organism. The unique effects of the regulatory peptides of the oxoproline series (5-o-N...o-Pro-His-Pro-NH₂, 5-oxo-Pro-Trp-Pro and 5-oxo-Pro-Arg-Pro or 5-o-N...o-Pro-His-Pro-NH₂, Pyr-Trp-Pro and Pyr-Arg-Pro) have been found in rats with hypercholesterolemia (metabolic syndrome). Multiple intranasal of these peptides to animals with developed hypercholesterolemia increased anticoagulant, fibrinolytic and antiplatelet potential of the blood and simultaneously lowered increased concentrations of total cholesterol, low-density lipoprotein cholesterol and triglycerides. In addition, they contributed to the normalization of blood glucose levels. A week after the last administration of these peptides, the hypocholesterolemic, normoglycemic and anticoagulant effects persisted. The relationship between the structure of peptides of the oxoproline series and their functional properties is discussed. A conclusion is made about the prospects of further studies of oxoproline peptides as drugs that combine antithrombotic effects with the improvement of fat metabolism in the body.

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10. *Kuznetsova T.A., Ivanushko L.A., Persiyanova E.V., Shutikova A.L., Ermakova S.P., Khotimchenko M.Yu., Besednova N.N.*

Evaluation of adjuvant effects of fucoidane from brown seaweed *Fucus evanescens* and its structural analogues for the strengthening vaccines effectiveness.

The use of sulfated polysaccharides from brown seaweed *Fucus evanescens* as adjuvants (native fucoidan in combination with polyphenols, fucoidan without polyphenols, a product of enzymatic hydrolysis of fucoidan) stimulated the formation of specific antibodies to the surface antigen of the hepatitis B virus (HBs-AG). Immunization of mice with vaccine compositions containing HBs-AG and fucoidan samples resulted in increasing the serum level of the pro-inflammatory (TNF- α , IFN- γ , IL-2) cytokines. Increased production of these cytokines was detected in the culture of splenocytes additionally stimulated in vitro by fucoidans or phytohemagglutinin. The adjuvant effect of fucoidan and its structural modifications was comparable to that of the traditional licensed adjuvant aluminum hydroxide. The obtained results indicate a promising use of sulfated polysaccharides from *F. evanescens* as vaccine adjuvants.

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11. Maslova O.V., Senko O.V., Efremenko E.N.

The influence of enzymatic removal of chlorpyrifos from feed grain-mixture on the biochemical parameters of rat blood.

Organophosphorus pesticides (OP) are used to protect crops from pests. Treatment of plants and animals with pesticides can be done during their growth or creation of conditions necessary for the long-shelf life of the agricultural products. Currently, there are many remedies for prevention and removal of intoxication consequences developed under the action of OP in living organisms. The development of biologics for the degradation of OP and biotechnologies for their application in agriculture is relevant. New biologics based on the stabilized forms of such enzyme as hexahistidine-tagged organophosphorus hydrolase (His6-OPH) in the form of nano-sized particles were tried for OP detoxification. These biologics (enzyme-polyelectrolyte complexes, EPC) were obtained in accordance to previously developed procedure by mixing solutions of His6-OPH and polyanion under certain conditions. The main purpose of this work was to evaluate the usage efficiency of EPC based on His6-OPH and polyglutamic acid for OP detoxification by analyzing biochemical blood parameters of rats consumed the grain-mixture containing chlorpyrifos. The experiment was conducted using female Sprague Dawley albino rats. Treatment of feeding grain-mixture initially containing chlorpyrifos (48 mg/kg of the mixture) with EPC based on His6-OPH (1000 U/kg of the mixture) for 24 h was the most effective. The results showed that rats from the group consuming food after enzymatic removal of chlorpyrifos, had comparable acetyl cholinesterase activity in blood of rats consuming pure food (without any OP intoxication).

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12. Ivanova E.A., Zolotov N.N., Kapitsa I.G., Pozdnev V.F., Valdman E.A., Voronina T.A.

Effect of afobazole and levodopa on the activity of proline-specific proteinases and adenosine deaminase in blood serum and brain structures of rats with experimental Parkinson's syndrome induced by systemic administration of rotenone.

Rats with experimental Parkinson's syndrome induced by seven-day intraperitoneal administration of rotenone at a dose of 2.75 mg/kg have an increased activity of prolylendopeptidase (EC 3.4.21.26, PREP) in blood serum and a decreased activity of adenosine deaminase (EC 3.5.4.4, ADA) in serum and in the prefrontal cortex. PREP and ADA activity in other brain structures (in the striatum, hypothalamus and hippocampus) did not change; dipeptidyl peptidase IV activity (EC 3.4.14.5, DPP-4, CD26) also remained constant in serum and in all the brain structures investigated. Afobazole and levodopa, which exhibit antiparkinsonian activity in this model of Parkinson's syndrome, decrease elevated PREP activity in serum and increase reduced ADA activity in the prefrontal cortex of rats with the experimental pathology. Meanwhile, treatment with the study drugs was associated with a decrease of ADA activity in the other brain structures.

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13. Bogdanov K.V., Motorin D.V., Nikulina T.S., Pisotskaya O.S., Babenetskaya D.V., Mirolyubova Y.V., Volkova O.Y., Zaritskiy A.Y.

Donor chimerism and minimal residual disease monitoring in leukemia patients after allo-HSCT.

In present research the comparative analysis of donor chimerism (DC) using different tests was performed to improve the diagnostic tool in patients with malignant hematological disorders after allo-HSCT. The RBC antigen typing, identification of ABO blood type and quantitative analysis of InDel-, STR-, Y-polymorphisms were carried out for detection of DC. In addition, the expression of well-known oncogenes and CD-markers for monitoring MRD was evaluated to predict relapse and clinical outcome. According to our research, the analysis of InDel polymorphism using AlleleSEQR-PCR is more sensitive test for estimation of DC as compared with other assays. Moreover, the sensitivity of AlleleSEQR-PCR may be increased after isolation of the CD34 cell population in bone marrow. Nevertheless, observation of high levels in DC ($\geq 95\%$) in some leukemia patients (ALL, Ph+, bcr-abl/p190+) during first 6 months after HSCT cannot exclude the possibility of relapse. Thus, the combined monitoring of both DC (InDel) and MRD (oncogenes, WT1 and CD-markers) is a more advisable and useful test in managing hematologic malignancies and predicting relapse risk after allo-HSCT.

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14. Vasilenko M.A., Kirienkova E.V., Skuratovskaya D.A., Zatolokin P.A., Mironyuk N.I., Litvinova L.S.

The chemerin production changes in obese patients with different carbohydrate metabolism state.

Chemerin is a mediator of adipose tissue involved in the regulation of many processes, including lipogenesis, and inflammatory response. The role of chemerin in the development of insulin resistance has been insufficiently studied and needs detailed understanding. The aim of the study was to investigate chemerin production in obese patients with different states of carbohydrate metabolism. The study included 155 patients with a diagnosis of obesity; 34 patients with overweight. The control group 1 consisted of 43 conditionally healthy donors who did not have obesity. For comparison of the results of a study to determine the levels of tissue-specific mRNA expression of the genes IL-6, TNF- α , RARRES2, (encoding IL-6, TNF- α and chemerin) in adipose tissue introduced a control group 2 – 30 patients without obesity. Study on the relative level of mRNA expression of the genes IL-6, TNF- α and RARRES2 (encoding IL-6, TNF- α and chemerin) was carried out using real time PCR. Concentrations of IL-6, TNF- α , and chemerin were measured in serum/plasma using an enzyme-linked immunosorbent assay (ELISA). We found significant differences in the plasma level of chemerin and tissue-specific features of RARRES2 gene expression in obese patients, depending on the degree of obesity and the state of carbohydrate metabolism. Multidirectional associations of RARRES2 gene expression with TNF- α and IL-6 genes in adipose tissues of different localization are shown: in obese patients (BMI ≥ 40 kg/m²) without type 2 diabetes – negative, and type 2 diabetes – positive. Identified

relationship chemerin plasma content and the expression level of its gene in biopsies with various parameters of carbohydrate and lipid metabolism, proinflammatory molecules indicate chemerin involved in metabolic and immune processes in obesity.

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