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1. Besednova N.N., Makarenkova I.D., Zvyagintseva T.N., Imbs T.I., Somova L.M., Zaporozhets T.S.

Antiviral action and pathogenetic targets for seaweed sulfated polysaccharides in herpesvirus infections.

The review summarizes results of studies of effects of sulfated polysaccharides from seaweed on herpesviruses and the course of herpesvirus infections. Importance of this problem is determined by the prevalence of herpesviruses that can persist in the human body and demonstrate a high degree of immune mimicry and resistance to antiviral agents. A wide range of physiological action of sulfated polysaccharides, receptor agonists of innate and adaptive immune cells, which possess potent antiviral, antioxidant and anti-inflammatory activities, open the possibility of their use for creation of new generation pharmacological substances and agents with associated activity for the treatment of herpesvirus infections.

DOI: 10.18097/PBMC20166203217

2. Kim Y.S., Kaidina A.M., Chiang J.H., Yarygin K.N., Lupatov A.Yu.

Molecular markers of cancer stem cells verified in vivo.

This systematic review aims to analyze molecular markers of cancer stem cells. Only studies that confirmed tumor-initiating capacity of this population by in vivo assay in immunodeficient mice were included. Final sample of papers that fully correspond with initial aim consists of 97 original studies. The results of their analysis reveal that markers commonly used for cancer stem cells deriving were as follows: CD133, Đ¡D44, ALDH, CD34, CD24 and EpCAM. The review also contains description of molecular features of some cancer stem cell markers, modern approaches to cancer treatment by targeting this population and brief assessment of cancer stem cell theory development.

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3. Zhdanov D.D., Vasina D.A., Orlova V.S., Gotovtseva V.Y., Bibikova M.V., Pokrovsky V.S., Pokrovskaya M.V., Aleksandrova S.S., Sokolov N.N.

Apoptotic endonuclease EndoG induces alternative splicing of telomerase catalytic subunit hTERT and death of tumor cells.

Telomerase activity is known to be regulated by alternative splicing of its catalytic subunit hTERT (human Telomerase Reverse Transcriptase) mRNA. Induction of non-active spliced hTERT leads to inhibition of telomerase activity. However, very little is known about the mechanism of hTERT mRNA alternative splicing. The aim of this study was to determine the role of apoptotic endonuclease EndoG in alternative splicing of hTERT and telomerase activity. Strong correlation was found between expression of EndoG and hTERT splice-variants in 12 colon cancer cell lines. Overexpression of EndoG in Đ¡Đ°Đ¡Đ¾-2 cells downregulated the expression of active full-length hTERT variant and upregulated non-active spliced variant. Reduction of full-length hTERT caused downregulation of telomerase activity, dramatically shortening of telomeres length during cell divisions, converting cells to the replicative senescence state, activation of apoptosis and finally cell death. These data indicated the participation of EndoG in alternative splicing of mRNA of telomerase catalytic subunit, regulation of telomerase activity and cell fate.

DOI: 10.18097/PBMC20166203239

4. Artyukhov V.G., Kalaeva E.A., Putintseva O.V., Polyubez'eva A.I.

The modification of structural and functional properties of human hemoglobin induced by nitroglycerin under different oxygen regime conditions.

Human oxyhemoglobin exhibits high resistance to nitroglycerin during incubation of the protein with this compound for 0.3-3 h. Prolonged exposure (24 h) leads to activation of methemoglobin production. In the presence of nitroglycerin hemoglobin molecules undergo rapid oxidation during deoxygenation with formation of methemoglobin as the terminal product of human oxyhemoglobin interaction with nitroglycerin. The scheme of interaction processes of oxyhemoglobin with nitroglycerin in different conditions of oxygen regime is proposed. Partially deliganded hemoglobin plays the leading role in the initiation of hemoglobin oxidation processes.

DOI: 10.18097/PBMC20166203251

5. Yunusova E.S., Sadykov E.S., Sultanalieva N.M., Shkinev A.V.

Fibrinogen/fibrin-specific enzymes from copperhead (Agkistrodon halys halys) and cobra (Naja oxiana eichwald) snake venoms.

Ability of fractions of cobraâ€™s (Naja oxiana Eichwald) and copperhead snakeâ€™s (Agkistrodon halys halys) venoms to hydrolyze fibrinogen/fibrin was studied. In cobraâ€™s snake a component with molecular mass of nearly 60 kDa was found to hydrolyze a-chain of fibrinogen but failed to hydrolyze casein/azocasein and fibrin. A fibrinogen-specific metalloproteinase, the enzyme was inhibited by EDTA. Cobraâ€™s venom reduced the mass of donorâ€™s fresh blood clots. The copperhead snakeâ€™s venom and the fractions obtained by gel-filtration (HW-50) and ion exchange chromatography (DEAE-650) were found to hydrolyze casein/azocasein, a- and b-chains of fibrinogen/fibrin and donorâ€™s blood clots. The results from the study of the venom and proteolytically active fractions are the evidence for a thrombolytic potential in a copperhead snakeâ€™s venom.

DOI: 10.18097/PBMC20166203259

6. Nikiforova Z.N., Taipov M.A., Kudryavcev I.A., Shevchenko V.E.

The connection of miR-21 and miR-155 with regulation of 15-HPGDH mRNA in human breast cancer cells.

Breast cancer is the most frequent cancer and the leading cause of cancer-related deaths in women worldwide. We determined the expression of COX2, COX1, 15-HPGDH mRNA and miRNAs (miR-21, miR-155) in three estrogen positive human breast cancer cell lines (MCF-7, BT-474, ZR-75-1). According to the results of three independent experiments the amount of COX1 and COX2 mRNA was significantly higher in the ZR-75-1 than in MCF-7 and BT-474 cells. Levels of total 15-HPGDH; functional 15-HPGDH mRNA in BT-474 cell line were lower than in MCF-7 and ZR-75-1 ones. The synthesis of 15-HPGDH enzyme in BT-474 line was blocked at the nuclear immature pre-mRNA processing level. miR-155 expression level was significantly lower than miR-21 in breast cancer cell lines. Correlations between the dysregulation of miR-21, miR-155 and 15-HPGDH, COX-1, COX-2 mRNA were identified. Expression of miR-21 was high in MCF-7, ZR-75-1 and BT-474 cell lines. Our results show that miR-21 and miR-155 regulate activity of several genes in cancer cells, their effect on the individual genes was in some cases cumulative. Based on our results, we concluded that miR-21, miR-155 suppress the work of tumor suppressor gene 15-HPGDH and induce potential oncogene COX-2 that promotes cell malignancy and metastasis of breast cancer.

DOI: 10.18097/PBMC20166203265

7. Kozlova N.I., Morozevich G.E., Ushakova N.A., Gevorkian N.M., Berman A.E.

Implication of integrin alpha5beta1 signal pathways in proliferation and apoptosis of MCF-7/Dox human breast carcinoma cells.

In MCF-7/Dox human breast carcinoma cells, down-regulation of integrin alpha5beta1 and inhibition of epidermal growth factor receptor (EGFR) markedly reduced rates of cell proliferation. Mitotic cycle analysis showed that alpha5beta1 down-regulation resulted in cell cycle arrest at the S phase, followed by a significant increase in the population of apoptotic cells (subG1 population). Inhibition of EGFR activity also caused cell cycle arrest at the S-phase but without any increase in the subG1 population. Down-regulation of alpha5beta1 and EGFR inhibition resulted in a significant decrease of cell content of the active (phosphorylated) forms of FAK and Erk protein kinases. The data obtained suggest that alpha5beta1 integrin is implicated in cell growth control via inhibition of apoptotic cell death and through EGFR activation.

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8. Zelenikhin P.V., Makeeva A.V., Nguen T.N., Siraj Y.A., Ilinskaya O.N.

Combined action of binase and bleomycin toward human lung adenocarcinoma cells.

Some microbial ribonucleases (RNases) demonstrate selective cytotoxic effect against a wide range of tumor cells. In this context combined use of cytotoxic RNases in complex therapy with other chemotherapeutic agents appears to be especially promising. In this study we have investigated the apoptosis-induced effect of Bacillus pumilus RNase (binase) in combination with known anti-tumor antibiotic bleomycin on human lung adenocarcinoma A549 cells. The combined effect of high concentrations of these agents did not have any mutual increase in their apoptosis-induced action, while a combination of non-apoptotic concentrations resulted in the increase of the proportion of apoptotic cells up to 22% as compared with individual effect of bleomycin (6%) and binase (12%) used separately. These results indicate that binase and bleomycin are effective in combination of their low concentrations and ineffective in combination of their high concentrations.

DOI: 10.18097/PBMC20166203279

9. Miroshnikova V.V., Panteleeva A.A., Bazhenova E.A., Demina E.P., Usenko T.S., Nikolaev M.A., Semenova I.A., Neimark A.E., He J., Belyaeva O.D., Berkovich O.A., Baranova E.I., Pchelina S.N.

Regulation of ABCA1 and ABCG1 gene expression in the intraabdominal adipose tissue.

Tissue specific expression of genes encoding cholesterol transporters ABCA1 and ABCG1 as well as genes encoding the most important transcriptional regulators of adipogenesis â€“ LXRa, LXRb, PPARg and RORa has been investigated in intraabdominal adipose tissue (IAT) samples.A direct correlation between the content of ABCA1 and ABCG1 proteins with RORa protein level ($r=0.480$, $p<0.05$; $r=0.435$, $p<0.05$, respectively) suggests the role of the transcription factor RORa in the regulation of IAT ABCA1 and ABCG1 protein levels. ABCA1 and ABCG1 gene expression positively correlated with obesity indicators such as body mass index (BMI) ($r=0.522$, $p=0.004$; $r=0.594$, $p=0.001$, respectively) and waist circumference ($r=0.403$, $p=0.033$; $r=0.474$, $p=0.013$, respectively). The development of obesity is associated with decreased IAT levels of RORa and LXRb mRNA ($p=0.016$ and $p=0.002$, respectively). These data suggest that the nuclear factor RORa can play a significant role in the regulation of cholesterol metabolism and control IAT expression of ABCA1 and ABCG1, while the level of IAT LXRb gene expression may be an important factor associated with the development of obesity.

DOI: 10.18097/PBMC20166203283

10. Scherbakov A.M., Levina I.S., Kulikova L.E., Fedyushkina I.V., Skvortsov V.S., Veselovsky A.V., Kuznetsov Y.V., Zavarzin I.V.

Cytotoxic activity and molecular modeling of progestins - pregna-D'-pentarans.

The cytotoxic activity of synthetic progestins (pregna-D'-pentaranes) II-V full agonists of the progesterone receptor (PR) for PR-positive and PR-negative cells of human breast carcinoma was studied. These compounds were more active in the PR-positive MCF-7 cells than in the PR-negative MDA-MB-453 cells. Cytotoxic effects of tested compounds against normal epithelial MDCK cells were not found. Molecular modeling of studied steroids with PR showed that all progestins with close energy values can bind to the ligand binding domain (LBD) of PR and the magnitude of the energy exceeds the value estimated for the progesterone molecule. Thus, the studied progestins are active against different molecular subtypes of breast cancer and represent a promising class of chemical compounds for oncology.

DOI: 10.18097/PBMC20166203290

11. Maksimenko A.V., Vavaeva A.V., Zvyagintseva M.A., Abramov A.A., Timoshin A.A., Vavaev A.V., Lakomkin V.L.

Protective action figurations for superoxide dismutase - chondroitin sulfate - catalase bienzyme conjugate after its medicative administration

in endotoxin shock.

Previously it found that the bienzymatic conjugate superoxide dismutase-chondroitin sulfate, catalase (SOD-CHS-CAT) increased the survival rate of rats with endotoxic shock caused by the administration of lipopolysaccharide (LPS). This effect was observed both in preventive (before LPS) and therapeutic conjugate administration (after the administration of LPS). This study shows that the development of endotoxic shock is accompanied by increased levels of NO in the liver, lungs, kidneys, heart; administration of the SOD-CHS-CAT conjugate insignificantly influenced this parameter. At the same time, the changes in blood urea and creatinine suggest the protective effect of the conjugate on renal function, while diverse changes in biochemical parameters studied complicate the formation of the agreed conclusions on the state of other organs.

DOI: 10.18097/PBMC20166203295

12. Shatova O.P., Butenko Eu.V., Khomutov Eu.V., Kaplun D.S., Sedakov I.Eu., Zinkovych I.I.

Metformin impact on purine metabolism in breast cancer.

Large-scale epidemiological and clinical studies have demonstrated the efficacy of metformin in oncology practice. However, the mechanisms of implementation of the anti-tumor effect of this drug there is still need understanding. In this study we have investigated the effect of metformin on the activity of adenosine deaminase and respectively adenosinergic immunosuppression in tumors and their microenvironment. The material of the study was taken during surgery of breast cacer patients receiveing metformin, and also patients which did not take this drug. The adenosine deaminase activity and substrate (adenosine) and products (inosine, hypoxanthine) concentrations were determined by HPLC. Results of this study suggest that metformin significantly alters catabolism of purine nucleotides in the node breast adenocarcinoma tisue. However, the metformin-induced increase in the adenosine deaminase activity is not sufficient to reduce the level of adenosine in cancer tissue. Thus, in metformin treated patients the adenosine concentration remained unchanged, and inosine and hypoxanthine concentration significantly increased.

DOI: 10.18097/PBMC20166203302

13. Kostryukova L.V., Sanzhakov M.A., Ignatov D.V., Prozorovskyi V.N., Druzhilovskaya O.S., Kasatkina E.S., Medvedeva N.V., Ipatova O.M.

The increase in receptor-mediated endocytosis of drugs in the composition of nanoparticles with the address fragment.

It is known that disorders in the cell functioning of the organs/tissues is accompanied by increased expression of certain receptors. A modern approach to improve the specificity of the drug accumulation in the affected area is to construct the delivery nanosystems with the address fragments. Active tagged transport may help to reduce the dose of the drug, minimizing the impact on healthy cells and organs (reduced adverse events). This approach is particularly important in oncology because of the high toxicity of the drugs used. In this work we have obtained and characterized the pharmaceutical composition of doxorubicin and chlorine e6 into colloidal nanoparticles with synthesized previously targeted conjugates based on folic acid and biotin. On the cell culture Hep G2 it was shown an increase in the internalization of drugs when they were introduced in the incubation medium in the form of drug compositions with transport nanosystems and targeted fragments.

DOI: 10.18097/PBMC20166203306

14. Zavodnik I.B.

Mitochondria, calcium homeostasis and calcium signaling.

Đ¡Đ°2+ is a very important and versatile intracellular signal which controls numerous biochemical and physiological (pathophysiological) processes in the cell. Good evidence exists that mitochondria are sensors, decoders and regulators of calcium signaling. Precise regulation of calcium signaling in the cell involves numerous molecular targets, which induce and decode changes of Đ¡Đ°2+ concentrations in the cell (pumps, channels, Đ¡Đ°2+-binding proteins, Đ¡Đ°2+-dependent enzymes, localized in the cytoplasm and organelles). Mitochondrial Đ¡Đ°2+ uniporter accumulates excess of Đ¡Đ°2+ in mitochondria, while Na+/Đ¡Đ°2+- and H+/Đ¡Đ°2+-antiporters extrude Đ¡Đ°2+ in the cytoplasm. Mitochondrial Đ¡Đ°2+ overloading results in formation of mitochondria permeability transition pores which play an important role in cell death under many pathological conditions. Mitochondria regulate Đ¡Đ°2+ homeostasis and control important cellular functions such as metabolism, proliferation, survival. Identification of cellular and mitochondrial Ca2+ transporters and understanding their functional mechanisms open up new prospects for their using as therapeutic targets

DOI: 10.18097/PBMC20166203311

15. Grigorieva D.V., Gorudko I.V., Kostevich V.A., Sokolov A.V., Buko I.V., Vasilyev V.B., Polonetsky L.Z., Panasenko O.M., Cherenkevich S.N.

Myeloperoxidase activity in blood plasma as a criterion of therapy for patients with cardiovascular disease.

A significant increase in the myeloperoxidase (MPO) activity has been found in plasma of patients with stable angina and with acute coronary syndrome (ACS) in comparison with the control group. MPO concentration was significantly increased in plasma of ACS patients. Reduced MPO activity in the treated ACS patients correlated with a favorable outcome of the disease. Generally, changes in plasma MPO concentration coincided with changes in lactoferrin concentration thus confirming the role of neutrophil degranulation in the increase of plasma concentrations of these proteins. The increase in MPO activity was obviously determined by modification of the MPO protein caused by reactive oxygen species and halogen in the molar ratio of 1 : 25 and 1 : 50. The decrease in plasma MPO activity may be associated with increased plasma concentrations of the physiological inhibitor of its activity, ceruloplasmin, and also with modification of the MPO protein with reactive oxygen species and halogen at their molar ratio of 1 : 100 and higher. Thus, MPO activity may be used for evaluation of effectiveness of the treatment of cardiovascular diseases.

DOI: 10.18097/PBMC20166203318

16. Dukova O.A., Kotlovsky M.Yu., Pokrovsky A.A., Suvorova E.V., Shivrina T.G., Krasnov E.A., Efremov A.A.

Identification and quantitative determination of baclofen in human blood by HPLC with mass spectrometry detection.

A method of identification and quantitative determination of baclofen in blood by HPLC with mass spectrometry detection has been developed. It is characterized by high sensitivity, specificity, linearity, accuracy, reproducibility, and a low detection for quantitative determination. The method has been used for diagnostics of acute baclofen poisoning in patients.

DOI: 10.18097/PBMC20166203325

17. Speranskii A.I., Kostyuk S.V., Kalashnikova E.A., Veiko N.N.

Enrichment of extracellular DNA from the cultivation medium of human peripheral blood mononuclears with genomic CpG rich fragments results in increased cell production of IL-6 and TNF-a via activation of the NF-kB signaling pathway.

Previously, it was found that blood plasma extracellular DNA (ecDNA) of patients with rheumatoid arthritis (RA) is enriched with CpG-rich genomic DNA fragments, which contain TLR9 ligands (Veiko et al., 2006). In this study we have demonstrated that ecDNA of a RA patient and model fragments added to a cultivation medium of peripheral blood mononuclear cells (PBMC) of healthy donors stimulate expression of genes for the TLR9â€“MyD88â€“NF-kB signaling pathway; this leads to a significant increase in concentrations of the proinflammatory cytokines IL-6 and TNF-a in the cultivation medium. Human genomic DNA non-enriched with the CpG sequences did not stimulate IL-6 and TNF-a synthesis in PBMC. A scheme explaining the potential role ecDNA in the induction and maintenance of increased levels of the proinflammatory cytokines under conditions damaging the human cells has been proposed.

DOI: 10.18097/PBMC20166203331

18. Denisenko Y.K., Novgorodtseva T.P., Zhukova N.V., Antonuk M.V., Lobanova E.G., Kalinina E.P.

Association of fatty acid metabolism with systemic inflammatory response in chronic respiratory diseases.

We examined composition of plasma non-esterified fatty acids (NFAs), erythrocyte fatty acids, levels of eicosanoids in patients with asthma and chronic obstructive pulmonary disease (COPD) with different type of the inflammatory response. The results of our study show that asthma and COPD in remission are associated with changes in the composition NFAs of plasma, FA of erythrocytes, level eicosanoid despite the difference in the regulation of immunological mechanisms of systemic inflammation. These changes are characterized by excessive production of arachidonic acid (20:4n-6) and cyclooxygenase and lipoxygenase metabolites (thromboxane B2, leukotriene B4) and deficiency of their functional antagonist, eicosapentaenoic acid (20:5n-3). The recognized association between altered fatty acid composition and disorders of the immune mechanisms of regulation of systemic inflammation in COPD and asthma demonstrated the important role of fatty acids and their metabolites in persistence of inflammatory processes in diseases of the respiratory system in the condition of remission.

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