# Biomeditsinskaya Khimiya

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

2013 volume 59 issue 3

*1. Berman A.E., Kozlova N.I., Morozevich G E.*

**Integrins as a potential target for targeted anticancer therapy.**

The review briefly summarizes information of structure of integrins and their involvement in the development and malignant progression of tumors. Special attention is paid to approaches based on modification of functional properties of integrins that prevent/antagonize tumor growth and progression; these approaches developed in modern experimental biology have certain perspective in clinical application.

DOI: 10.18097/pbmc20135903239

*2. Bozrova S.V., Levitsky V.A., Nedospasov S.A., Drutskaya M.S.*

**Imiquimod: the biochemical mechanisms of immunomodulatory and anti-inflammatory activity.**

Imidazoquinolins represent a new group of compounds that recently entered into clinical practice as anti-tumor and anti-viral immune modulators. They are low molecular weight synthetic guanosine-like molecules. Although imiquimod, the most widely used imidazoquinolin, is recommended for the treatment of several forms of skin cancer and papillomas, the molecular mechanisms of its action are not fully understood. In particular, imiquimod has been characterized as a specific agonist of Toll-like receptor 7 (TLR7) and is widely used in this capacity in a large number of experimental studies and clinical trials. However, detailed analysis of the published data with the use of imiquimod, suggests that its biological activity can not be explained only by interaction with TLR7. There are indications of a direct interaction of imiquimod with adenosine receptors and other molecules that regulate the synthesis of cyclic adenosine monophosphate. A detailed understanding of the biochemical basis of imiquimod immunomodulating and antitumor effect will increase its clinical effectiveness and accelerate the development of new drugs with similar but improved medical properties. This review summarizes the published data concerning the effects of imiquimod on a variety of intracellular biochemical processes and signaling pathways.

DOI: 10.18097/pbmc20135903249

*3. Fedosov A.E., Moshkovskii S.A., Kuznetsova K.G., Olivera B.M.*

**Conotoxins: from the biodiversity of gastropods to new drugs.**

A review describes general trends in research of conotoxins that are peptide toxins isolated from sea gastropods of the Conus genus, since the toxins were discovered in 1970 . There are disclosed a conotoxin classification, their structure diversity and different ways of action to their molecular targets, mainly, ion channels. In the applied aspect of conotoxin research, drug discovery and development is discussed, the drugs being based on conotoxin structure. A first exemplary drug is a ziconotide, which is an analgesic of new generation.

DOI: 10.18097/pbmc20135903267

*4. Severina I.S., Schegolev A.Yu., Medvedev A.E.*

**Potentiation of NO-dependent activation of soluble guanylyl cyclase by 5-nitroisatin and antiviral preparatation arbidol.**

Isatin (indole-dione) is an endogenous indole that exibits a wide range of biological and physiological activity. The influence of isatin derivatives 5-nitroisatin and arbidol (an antiviral preparatation) on spermine NONO-induced activation of human platelet soluble guanylyl cyclase was investigated. 5-nitroistnin and arbidol had no effect on basal activity, but synergistically increased in a concentration-dependent manner the spermine NONO-induced activation of this enzyme. 5-Nitroisatin and arbidol, like YC-1, sensitized guanylyl cyclase towards nitric oxide (NO) and produced a leftward shift of the spermine NONO concentration response curve. At the same time both compounds used did not influence the activation of guanylyl cyclase by YC-1 and did not change the synergistic increase of spermine NONO-induced activation of soluble guanylyl cyclase in the presence of YC-1. This suggests that 5-nitroisanin and arbidol did not compete with YC-1. Addition of isatin did not change the synergistic increase in the spermine NONO-induced guanylyl cyclase activation by 5-nitroisatin and arbidol and did not influence a leftward shift of spermine NONO concentration response curve produced by these compounds. These data suggest lack of competitive interaction between isatin and both its derivatives used.

DOI: 10.18097/pbmc20135903295

*5. Abakumova O.Y., Podobed O.V., Belayeva N.F., Tochilkin A.I.*

**Anticancer activity of oxovanadium compounds.**

Cytotoxic and antitumor activity of the biligand vanadyl derivative of L-malic acid (bis(L-malato)oxovanadium(IV) (VO(mal) ) was investigated in comparison with inorganic vanadium(IV) compound - vanadyl sulfate (VOSO ) and also with oxovanadium monocomplex with L-malic acid (VO(mal)) and vanadyl biscomplex with acetylacetonate. In this purpose the effect of vanadyl compounds on growth of normal human skin fibroblasts and tumor cells of different lines: mouse fibrosarcoma (L929), rat pheochromocytome (PC12), human liver carcinoma (HepG2), virus transformated mouse fibroblast (NIN 3T3), virus transformated cells of human kidney (293) were investigated. The results showed that VO(mal) was not toxic for normal human skin fibroblasts but considerably inhibited growth of cancer cells in culture. Cytotoxic antitumor effect of vanadium complexes was found to be dependent Ð¾n incubation time and concentration and on type of cells and nature of ligands of the central group of the complex (VO2+). These studies provide evidence that VO(mal) may be considered as a potential antitumor agent due to its low toxicity in non-tumor cells and significant anticancer activity.

DOI: 10.18097/pbmc20135903305

*6. Fedyushkina I.V., Stulov S.V., Dugin N.O., Misharin A.Yu., Mehtiev A.R., Morozevich G.E., Veselovsky A.V.*

**Molecular modeling of interaction of 17(20) and 17(20) E-pregna-5,17(20)-dien-21-oyl amides with the nuclear receptor LXRb.**

Aiming the search of novel regulators of lipid metabolism and their potential targets, in this study we performed molecular modeling of eight isomeric 17(20) Z - and 17(20) Ð• -pregna-5,17(20)-dien-21-oyl amides differing in structure of the amide moiety. Analysis of the low energy Ñ•onformers revealed that all 17(20) E -isomers had three main energy minima (corresponding to values of the dihedral angle q (Ð¡17=C20-C21=O) ~ 0Â°, ~ 120Â° and ~ 240Â°), the most occupied minimum was found to correspond to q ~ 0Â°; while 17(20) Z -isomers had either one or two pools of low energy conformations. Molecular docking of these compounds to the ligand-binding site of the nuclear receptor LXRb (a potential target) indicates high probability of binding for Ð• -isomers and the absence of that for Z -isomers. Results of the molecular modeling were confirmed by an experiment in which stimulation of triglyceride biosynthesis in Hep G2 cells in the presence of 17(20) Ð• -3b-hydroxypregna-5,17(20)-dien-21-Ð¾yl (hydroxyethyl)amide was demonstrated.

DOI: 10.18097/pbmc20135903321

*7. Milto I.V., Klimenteva T.K., Suhodolo I.V., Krivova N.A.*

**Prooxidant and antioxidant activity of blood plasma and histology of internal organs of rats after intravenous administration of magnetite nanoparticles.**

The effect of a single and multiple intravenous injections of a nanosized magnetite suspension on total prooxidant and antioxidant activity of blood plasma has been investigated by the method of luminol-dependent chemoluminescence. Magnetite nanoparticles possess dose-dependent prooxidant properties due to their iron atoms and at the same time their trigger compensatory activation of antioxidant systems in the rat blood plasma. After a single intravenous administration of magnetite the studied parameters of blood plasma returned to the normal level by the end of the experiment as due to removal of nanoparticles from the body. In the case of multiple administration of the magnetite suspension dose-dependent changes in the pro- and antioxidant plasma activity persist during the whole experiment. Accumulation of magnetite particles in the cells of the mononuclear phagocytic system in the ratsâ€™ liver, lungs and kidneys is associated with hemodynamic damages, local dystrophic and necrotic changes of parenchyma in these organs. After a single intravenous injection magnetite nanoparticles are identified in the rat organs for 40 days, but their number decreases by the end of the experiment.

DOI: 10.18097/pbmc20135903330

*8. Lupatov A.Yu., Gisina A.M., Karalkin P.A., Yarygin K.N.*

**Identification of "side population" associated with cancer stem cells by flow cytometry with violet laser.**

The possibility of identification of cancer stem cells "side population" in solid tumors by using the flow cytometer equipped with 405 nm violet laser was investigated. Ovarian cancer (Skov-3) and colon cancer (Colo 320) cell lines formed the "side population" after vital staining with Hoechst 33342. Analysis of cells isolated from tumor tissue of malignant melanoma and colorectal cancer, also revealed "side population" that was a result of the fluorescent dye exclusion. The percentage of melanoma cells included in the "side population" was the same as that of cells co-expressing cancer stem cells markers - CD34 and CD44. In contrast, the colon cancer "side population" was significantly smaller than the minor populations of colon cancer cells identified by either CD133 expression or exclusion of Rhodamine 123.

DOI: 10.18097/pbmc20135903339

*9. Vekshin N.L.*

**Photo-activity of actinomycins.**

Using actinomycins as an example, the possibility of increasing the anti-tumor activity of heterocyclic antibiotics due to photo-activation, has been studied. In model experiments with solutions of actinomycins, it was showed that actinomycins have a significant photochemical activity (of its own), changing by the binding to DNA in solution or in tumor cells. Photo-destruction of HeLa cells and the release of the antibiotic were observed.

DOI: 10.18097/pbmc20135903349

*10. Vasilyeva I.N., Zinkin V.N.*

**The value of low-molecular-weight DNA of blood plasma in the diagnostic of the patological processes of different genesis.**

The low-molecular-weight DNA appears in blood plasma of irradiated rats, and its content correlates directly with the irradiation dose. Cloning has shown, that enrichment of low-molecular-weight DNA with G+C content and features of its nucleotide sequences point to its ability to form rather stable nucleosomes. DNA obtained after irradiation of rats with principally different doses 8 and 100 Gy differed not only quantitatively, but also by content of the dinucleotides CpG and CpT; this suggests their origin from different sites of genome. For the first time it has been shown that exposure to low-frequency noise results in an increase of the contents of blood plasma low-molecular-weight DNA. In stroke patients blood concentrations of this DNA increased 3 days after the beginning of the acute period, and dynamics of its excretion differs in ischemic and hemorrhagic forms; in the case of ischemia low-molecular-weight DNA appears in cerebrospinal fluid. The chronic obstructive pulmonary disease in the state of remission is characterized by the decline of the level of low-molecular-weight DNA in the blood plasma unlike in the case of the chronic nonobstructive bronchitis. The clear dependence between formation and special features of the low-molecular-weight DNA fraction in blood plasma makes it possible to consider the low-molecular fraction as an universal index of apoptosis, which allows to distinguish basically different conditions of the body.

DOI: 10.18097/pbmc20135903358