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residues of TEM type were found. Several mutations are the key mutations that determine the extension of spectrum of substrates. However, roles of the most associated mutations, located far from active site, remain unknown. We have investigated the role of associated mutations in structure of b-lactamase TEM-72, which contain two key mutation (G238S, E240K) and two associated mutations (Q39K, M182T) by means of simulation of molecular dynamics. The key mutation lead to destabilization of the protein globule, characterized by increased mobility of amino acid residues at high temperature of modelling. Mutation M182T lead to stabilization protein, whereas mutation Q39K is destabilizing mutation. It seems that the last mutation serves for optimization of conformational mobility of b-lactamase and may influence on enzyme activity.
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*6. Sekridova A.V., Varizhuk A.M., Tatarinova O.N., Severov V.V., Barinov N.A., Smirnov I.P., Lazarev V.N., Klinov D.V., Pozmogova G.E.*

**Conformational polymorphysm of G-rich fragments of DNA ALU-repeats. I. Potential noncanonical structures.**

In this paper, we report results of systematic studies of conformational polymorphism of G-rich DNA fragments from Alu repeats. Alu retrotransposones are primate-specific short interspersed elements. Using the Alu sequence from the prooncogen bcl2 intron and the consensus AluSx sequence as representative examples, we determined characteristic Alu sites that are capable of adopting G-quadruplex (GQ) conformations (i.e., potential quadruplex sites â€“ PQSAlu), and demonstrated by bioinformatics methods that those sites are Alu-specific in the human genome. Genomic frequencies of PQSAlu were assessed (~1/10000 b.p.). The sites were found to be characteristic of young (active) Alu families (Alu-Y). A recombinant DNA sequence bearing the Alu element from the human bcl2 gene (304 b.p.) and its PQS-mutant (Alu-PQS) were constructed. The formation of noncanonical structures in Alubcl2 dsDNA and the absence of such structures in the case of Alu-PQS were shown using DMS-footprinting and AFM microscopy. Expression vectors bearing wild-type and mutant Alu insertions in the promoter regions were obtained, and the effects of these insertions on the expression of the reporter gene in Đ•Đ•Đš293 and HeLa cell lines were compared. Our findings on the spatial organization of Alu repeats may provide insight into the mechanisms of genomic rearrangements which underlie many oncological and neurodegenerative diseases.
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*7. Zhdanov D.D., Vasina D.A., Orlova E.V., Orlova V.S., Pokrovskaya M.V., Aleksandrova S.S., Sokolov N.N.*

**Apoptotic endonuclease EndoG regulates alternative splicing of human telomerase catalytic subunit hTERT.**

Human telomerase catalytic subunit hTERT is subjected to alternative splicing results in loss of its function and leads to decrease of telomerase activity. However, very little is known about the mechanism of hTERT pre-mRNA alternative splicing. Apoptotic endonuclease EndoG is known to participate this process. The aim of this study was to determine the role of EndoG in regulation of hTERT alternative splicing. Increased expression of b-deletion splice variant was determined during EndoG over-expression in CaCo-2 cell line, after EndoG treatment of cell cytoplasm and nuclei and after nuclei incubation with EndoG digested cell RNA. hTERT alternative splicing was induced by 47-mer RNA oligonucleotide in naked nuclei and in cells after transfection. Identified long non-coding RNA, that is the precursor of 47-mer RNA oligonucleotide. Its size is 1754 nucleotides. Based on the results the following mechanism was proposed. hTERT pre-mRNA is transcribed from coding DNA strand while long non-coding RNA is transcribed from template strand of hTERT gene. EndoG digests long non-coding RNA and produces 47-mer RNA oligonucleotide complementary to hTERT pre-mRNA exon 8 and intron 8 junction place. Interaction of 47-mer RNA oligonucleotide and hTERT pre-mRNA causes alternative splicing.
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*8. Kachesova P.S., Goroshinskaja I.A., Borodulin V.B., Shalashnaja E.V., Chudilova A.V., Nemashkalova L.A.*

**Effect of iron nanoparticles on free radical oxidation process in blood of rats with Pliss lymphosarcoma.**

The use of metal nanoparticles (NPs) for cancer treatment requires careful examination of their biological effects. The aim of this study was to determine parameters of oxidative processes in the blood of tumor-bearing animals treated with metallic iron NPs only. The markers of antioxidant status and accumulation of lipid peroxidation products were measured in erythrocytes and blood plasma of rats with Pliss lymphosarcoma (PLS) and intact rats. PLS animals were treated eight times with iron NPs (at a dose of 1.25 mg/kg bw (main group), rats of the control group received saline (0.3 ml). In control animals, an increase in malondialdehyde (MDA) was observed in red blood cells (RBC) by 45%; this was accompanied by compensatory increase in reduced glutathione (GSH) and catalase by 24% and 14.3%, respectively ($p<0.05$). In plasma an increase in MDA by 167.4% ($p<0.01$) and a decrease in oxidase activity of ceruloplasmin (CP) by 36.8% ($p<0.001$) were found. In the main group there was a decrease of accumulation of lipid peroxidation products in the blood. Intensity of detected changes depended on the antitumor effect: rats with growing LSP showed a tendency to the decrease in the RBC MDA level and normalization of plasma MDA; in animals with LSP regression this marker did not differ from normal values. In all animals of the main group the CP content was basically the same as in intact rats while GSH increased in the group without therapeutic effect (by 218.6%) and in the group with the effect by 69% (versus normal values; $p<0.01$). SOD activity in the rats with LSP growth significantly increased (by 42%), in the rats with regression decreased (by 30%) with subsequent normalization. Thus, administration of iron NPs caused activation of the antioxidant system in blood and a significant decrease in the manifestations of oxidative stress associated with tumor growth.
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*9. Popova T.N., Safonova O.A., Stolyarova A.O.*

**The effect of melaxen administration on the tissue oxidative status in rats with brain ischemia/reperfusion.**

Melaxen administration to rats with brain ischemia/reperfusion was accompanied by a decrease of the lactate level (an organ ischemia marker), biochemiluminescence parameters characterizing the intensity of free radical processes and total antioxidant activity, the content of lipid peroxidation products, activity of superoxide dismutase and catalase, as compared with the values determined in rats with induced brain ischemia/reperfusion. Activity of aconitate hydratase, a sensitive target of free radicals action, and the citrate level in the brain and blood serum of melaxen-treated animals changed towards control values of intact animals. It is assumed that the effect of melaxen is associated with implementation of the antioxidant and protective properties of melatonin, the melaxen constituent, under conditions of post-ischemic reperfusion injury, accompanied by oxidative stress development.

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*10. Rudnichenko Yu.A., Lukashevich V.S., Zalutsky I.V.*

**Experimental study of the influence of recombinant human lactoferrin on the levels of androgens and basic parameters of lipid and protein metabolism.**

System administration of human recombinant lactoferrin per os to rats for 2,5 months increased serum and testicular levels of total testosterone. The data correlated with the increase in free testosterone levels. These changes were accompanied by an increase of concentrations of steroidogenesis substrates (cholesterol, progesterone, and 17-OH progesterone) and a decrease of the estradiol content in blood serum. This resulted in the 3.6-3.8-fold increase of the testosterone/estradiol index. Basic parameters of lipid and protein were also studied. Results of this study suggest that lactoferrin administration causes activation of androgen synthesis and lipid metabolism.

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*11. Popova T.A., Perfilova V.N., Zhakupova G.A., Verovsky V.E., Ostrovskij O.V., Tyurenkov I.N.*

**The effect of sulodexide on placental mitochondria function in rats with experimental preeclampsia.**

Substitution of drinking water for 1.8% NaCl in pregnant rats caused a pronounced increase in arterial pressure by 24,3% and urinary protein by 117% to day 21 of pregnancy. State 4 respiration of isolated placental mitochondria in the group of negative control was 3- and 1.5-fold higher with malate/glutamate and succinate as substrates than in placental mitochondria isolated from uncomplicated pregnant animals. This led to a decrease of the respiratory control ratio. These results suggest that development of experimental preeclampsia is accompanied by mitochondrial dysfunction through uncoupling of oxidative phosphorylation. Daily administration of sulodexide to females with experimental preeclampsia (EP) per os at a dose of 30 LE during the whole period of gestation decreased manifestations of the disease as evidenced by a slight increase in blood pressure (by 8,6%) and less pronounces increase in urinary protein (by 58,9%). Sulodexide decreased development of mitochondrial dysfunction in EP rats as shown a decrease of non-stimulated ADP respiration with malate/glutamate and succinate (4.5- and 2.5-fold, respectively) as compared with the negative control group and the corresponding increase in the respiratory control ratio (2.5- and 1.5-fold, respectively). Thus, sulodexide reduces uncoupling of oxidative phosphorylation and enhances the functional activity of mitochondria in EP animals, possibly due to its antioxidant and endotelioprotective effects.

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*12. Shchelkonogov V.A., Sorokoumova G.M., Baranova O.A., Chekanov A.V., Klochkova A.V., Kazarinov K.D., Solovieva E.Y., Fedin A.I., Shvets V.I.*

**Liposomal form of lipoic acid: preparation and determination of antiplatelet and antioxidant activity.**

Optimal conditions for obtaining phosphatidylholine (PC) liposomes with lipoic acid (LA) are chosen that lead to the formation of nanoparticles with a size of 175Â¸284 nm with efficiency (extent) of inclusion of LA in liposomes equal 85% and characterized by a slow release of substance from the nanoparticles. The effect of â€œemptyâ€• liposomes and liposomal form of LA on platelet aggregation induced by arachidonic acid (AA) is established. It is found that liposomes with LÐ• inhibit platelet aggregation, caused by AÐ•, to 80%. In addition, it is shown that â€œemptyâ€• liposomes slightly (to 30%) suppress platelet aggregation, caused by AÐ•. The amount of TBA-sensitive products in samples of platelet-rich plasma (PRP) incubated with liposomal LA is determined. It is shown that LA in the composition of liposomes retains its antioxidant properties, and the amount of products of lipid peroxidation in platelet-rich plasma decreases in a dose-dependent manner when arachidonic acid is used as an inductor of platelet aggregation. It is assumed that the antiplatelet action of the liposomal form of LÐ• is induced by inhibition of the initiation of lipid peroxidation products caused by exogenous inducer AÐ•. It is supposed that, after additional research, the liposomal form of LA can be considered as a new drug in complex treatment of cerebral ischemia.

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*13. Mikhalchik E.V., Budkevich L.I., Piterskaya Yu.A., Penkov L.Yu., Astamirova T.S., Smolina N.V., Vakhrusheva T.V., Panasenko O.M.*

**The role of neutrophil myeloperoxidase in the development of inflammation after thermal skin burns.**

In the blood of children (n=16) with large thermal skin burns (> 20% of total body surface), luminol-dependent chemiluminescence (CL) of neutrophils stimulated with phorbol-12-myristate-13-acetate (PMA) and myeloperoxidase (MPO) activity in neutrophils and plasma were assayed in the early period (1-7 post-burn days). PMA-stimulated neutrophils in thermally injured patients produced higher CL than those in a reference group of healthy children (n=24), $p<0.01$. MPO activity was elevated in neutrophils and plasma in 40% and 57% of patients' blood samples, respectively. The albumin fraction isolated from plasma of burned patients enhanced the PMA-stimulated CL response of blood samples from healthy volunteer. Our results suggest that the acute inflammatory response induced by thermal injury involves activation of neutrophils and is accompanied by MPO release into the plasma. MPO-mediated modification of serum albumin induces its capacity to prime neutrophils and thus to enhance further inflammatory reaction.

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*14. Yakovlev A.A., Druzhkova T.A., Grishkina M.N., Guekht A.B., Gulyaeva N.V.*

**Caspase activity in peripheral blood mononuclear cells (PBMC) of patients with depression and anxiety of different severity.**

Though borderline psychiatric disorders (BPD) are quite common diseases, their pathogenesis remains obscure. Data from several groups and our previous results suggest that the pathological changes are typical not only for brain cells, but also for cells of the immune system. One of the evident illustrations of immune and nervous systems relationship in pathogenesis of mental diseases is the death of PBMC occurring in patients with depression. We have shown previously that activities of the caspases increase in some types of BPD. In this study, we have investigated caspase activities in PBMC of patients with BPD of different severity. It has been found that in severe depressive disorder activities of caspases were reduced either as compared to healthy controls or to patients with depression lesser severity. In contrast, in patients with severe anxiety activities of caspases were higher than in both control and patients with less severe forms of anxiety disorders. Thus, the study of caspase activity in PBMC makes it possible to differentiate between severe and mild forms of BPD.

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*15. Esmedlyaeva D.S., Alexeyeva N.P., Sapozhnikova N.V., Dyakova M.E., Perova T.L., Kiryukhina L.D., Zhuravlev V.Y.*

**The system of matrix metalloproteinases and their role in patients with pulmonary tuberculosis.**

The aim of this study was to examine the relationship between serum levels of parameters of the system metalloproteinase (MMP)/inhibitors with severity of infiltrative pulmonary tuberculosis (ITL), changes in examined parameters during the intensive phase treatment (IPT), as well as possibility of their use for prediction of IPT effectiveness, along with acute-phase proteins (AFP). The study included ITL patients which were subdivided into two groups (I and II) with different rates of reparative changes. It was shown that: 1) ITL is characterized by impairements in the system MMP/inhibitors: the levels of MMP-1, -9 increased, MMP-3, -8, TIMP-1 remained at the reference values and a 2-macroglobulin was low. 2) Changes of the parameters of the system MMP/inhibitors were associated with markers of severity and activity of the process: MMP-1, with the presence of destruction and sensitivity of the pathogen (Mycobacterium tuberculosis; MBT) to anti-TB drugs, MMP-9, with the volume of destruction, MMP-8 â€“ with activity of tuberculosis. 3) TIMP-1 and MMP-9 concentrations decreased during treatment in groups with different rates of reparative process, whereas proMMP-1, MMP-3,-8 remained unchanged. 4) Before and after IPT, the level of TIMP-1 was higher in the group of patients with slower rate of reparative processes. 5) After IPT the imbalance in the system MMP/inhibitor preserved thus suggesting continuation of the reparative process. 6) Use of combination of MMP and AFR is more informative in predicting efficacy of IPT.

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*16. Kisrieva Y.S., Petushkova N.A., Samenkova N.F., Kuznetsova G.P., Larina O.V., Zavialova M.G., Teryaeva N.B., Belyaev A.Y., Karuzina I.I.*

**Comparative proteome analysis of blood plasma of patients with early-stage chronic cerebral ischemia.**

In the present study, we explored the technology of liquid chromatography-mass spectrometry (HPLC-MS/MS) for the proteome analysis of blood plasma of patients with early chronic cerebral ischemia. Analysis of mass-spectrometer data carried out in automatic mode using the software Progenesis LS-MS. As a result of this study identified 43 proteins. The differences identified in the study group compared with the control in 7 proteins. It was found that in the early stages of chronic cerebral ischemia proteome changes in blood plasma affect proteins related to the immune system, the system for the maintenance of hemostasis and lipid metabolism.

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