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1. Proskuryakov S.Ya., Konoplyannikov A.G., Verkhovskii Yu.G., Ulyanova L.P., Tsyb A.F.

Where intestinal epithelial stem cells are localized? About molecular markers.

Using stem cells as an example the review considers a new history and methodology of search for stem cells (SC), found in tissues of adult Homo sapiens and Drosophila melanogaster organisms. These studies of SC resulted in several original hypotheses explaining their unusual features. Impressive progress recently achieved in this direction (2008-2010) is associated with employment of new methods of somatic recombination for long-term registration of various strains of differentiated cells, early and distant SC progeny. 1) Although anatomic localization of intestinal epithelium cells lacking marked morphological and biochemical differentiation markers (the lower third of intestinal and colon crypts) is known for about 40 years results of their experimental identification, isolation and detection of their functional characteristics still represent the subject for discussions. Particularly, it remains unclear, which SC are involved in crypt regeneration: the same as those involved into homeostatic renewal or their various subpopulations or early SC progenies acquired stem features by reprogramming? 2) In addition, most detected biochemical markers of potential SC are common for SC from other tissues of embryonic and mature organisms so it is possible to apply method developed for intestinal epithelium for their isolation. 3) Data on induction of intestinal epithelium polyps and neoplasias by mutations in genes encoding SC markers and identification of biochemical characteristics of potential SC in these tumors support the hypothesis of stem tumor cell origination from normal SC or their earliest progeny. In general, facts considered in this review may be useful for both development of optimal methods for the use of SC in cell therapy (as the source of humoral factors), regenerative medicine (as the source of differentiated cells for restoration of injured tissue), and also for targeted search of antitumor drugs (SC as the target) and preparations modifying genetic and epigenetic reactions of SC to genotoxic and stress treatments.

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2. Bonartzev A.P., Bonartzeva G.A., Shaitan K.V., Kirpichnikov M.P.

Poly(3-hydroxybutyrate) and biopolymer systems on the basis of this polyester.

Biodegradable biopolymers attract much attention in biology and medicine due to its wide application. The present review is designed to be a comprehensive source for research of biodegradable and biocompatible bacterial polymer, poly(3-hydroxybutyrate). This paper focuses on basic properties of biopolymer: biodegradability and biocompatibility, as well as on biopolymer systems: various materials, devices and compositions on the basis of biopolymer. Application of biopolymer systems based on poly(3-hydroxybutyrate) in medicine as surgical implants, in bioengineering as scaffold for cell cultures, and in pharmacy as drug dosage forms and drug systems is observed in the present review.

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3. Lisitskaya K.V., Eremina L.S., Ivanov A.V., Kovalyova M.A., Okhrits V.E., Toropygin I.Y., Kovalyov L.I., Shishkin S.S.

Study of Dj-1 protein in tissue specimens, cultured cells and serum of prostate cancer patients.

Two isoforms of Dj-1 protein were identified using a proteomic study in tissue specimens from two groups of patients with confirmed benign prostate hyperplasia (BPH) and prostate cancer (PCa). Dj-1 was also found in the cell lines Ð Ðį-3, DU-145, LNCaP, BPH-1, and the lowest level of Dj-1 was found in BPH-1. Immunochemical study (ELISA) of serum levels of Dj-1, Bcl-2, IGF-1 and IGFBP-3 proteins revealed statistically significant distinctions between two groups of patients (Ñ€=0,004, Mann-Whitney test) only for Dj-1. Taken together, these data suggest that Dj-1 protein is a perspective biomarker candidate for PCa.

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4. Shumyantseva V.V., Bulko T.V., Misharin A.Yu., Archakov A.I.

Screening of potential substrates or inhibitors of cytochrome P450 17a1 (CYP17a1) by electrochemical methods.

The electrochemical reduction of the recombinant form of human cytochrome P450 17A1 (CYP17A1) was investigated. Hemeprotein was immobilized on electrode modified with biocompatable nanocomposite material based on the membrane-like synthetic surfactant didodecyldimethylammonium bromide (DDAB) and gold nanoparticles. Analytical characteristics of DDAB/Au/CYP17A1 electrodes were investigated with cyclic voltammetry, square wave voltammetry, and differential pulse voltammetry. Analysis of electrochemical behaviour of cytochrome P450 17A1 was conducted in the presence of substrate pregnenolone (1), inhibitor ketoconazole (2), and in the presence of synthetic derivatives of pregnenolone: acetylpregnenolone (3), cyclopregnenolone (4), and tetrabrompregnenolone (5). Ketoconazole, azole inhibitor of cytochromes P450, blocked catalytic current in the presence of substrate pregnenolone (1). Compounds 3-5 did not demonstrate substrate properties towards electrode/CYP17A1 system. Compound 3 did not block catalytic activity towards pregnenolone, but compounds 4 and 5 inhibited such activity. Electrochemical reduction of CYP17A1 may serve as an adequate substitution of the reconstituted system which requires additional redox partners - for the exhibition of catalytic activity of hemoproteins of the cytochrome P450 superfamily.

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5. Fedoseeva L.A., Ryazanova M.A., Antonov E.V., Dymshiz G.M., Markel A.L.

Renin-angiotensin system gene expression in the kidney and in the heart in hypertensive ISIAH rats.

The content of mRNA of renin-angiotensin system (RAS) genes in the kidney and heart of hypertensive ISIAH and normotensive WAG rats was

measured by the real-time PCR. Statistically significant decrease of RAS gene mRNA was registered in the kidney of ISIAH rats, including Ren (by 45%), Đ•ce (43%), Đ•Đ¢1Đ• (34%), Đ¡ĐžĐ¥-2 (50%). In the myocardium Đ•Đ¢1Đ• mRNA expression decreased by 28% while Ace mRNA expression increased by 80%. These results demonstrate the reduction of renal RAS basal activity in the hypertensive ISIAH rats, and this allows us to consider the ISIAH rat, as a low-renin hypertensive strain.In support of this viewpoint, in the ISIAH rats, a two-fold increase in the connective tissue sodium concentration as well as statistically significant plasma sodium increase (from 136Â±0,25 Î¼mol/l in WAG to 139Â±0,3 Î¼mol/l in the ISIAH rats) were found. Our conclusion backed by a tendency of the ISIAH plasma aldosterone level decrease giving in sum a classical picture of a low-renin hypertensive state in the ISIAH rats.It was suggested that the formation of low-renin arterial hypertension in the ISIAH rats may depend on changes in kidney ion channels function. In addition, renal NO system alterations could be also involved in the pathogenesis of arterial hypertension in the ISIAH rats.
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6. Batikyan T.B., Hakopyan G.V., Lazyan M.P., Torgomyan T.P., Kazaryan R.A., Amirkhanyan E.S., Tadevosyan Yu.V.

Regularities of endogenous lipid metabolites formation in phorbol 12-miristate 13-acetate-stimulated peripheral blood lymphocytes at leukemia.

Regularities of biologically active lipid metabolites formation in dynamics (5, 10, 30, 60 s) by phorbol 12-miristate 13-acetate stimulation in [14C]palmitic acid have been investigated in normal and leukemia peripheral blood lymphocytes prelabeled with [14C]palmitate. In normal cells there was two-phase formation of 1,2-diacylglycerol (5, 30 s), lysophosphatidylcholine (10, 60 s), as well as free palmitic acid at 10 s of stimulation. Under the identical experimental conditions there was inhibition of investigated lipid release processes at early (5 and 10 s) stages of stimulation of leukemic lymphocytes. At later (30, 60 s) terms of these lymphocytes the activation, basically, similar to norm changes in the formation of palmitic acid-containing metabolites except free palmitic acid (the level of which raised only at 60 second of the post-stimulation) was found. Various protein kinases C are involved in the regulation of investigated lipid levels at certain stages of signal transduction both in norm, and in blast cells. Short-term (5, 10 s) activations of healthy donors lymphocytes are coupled to functioning of Đ¡Đ°2+-independent isoforms of protein kinase C. The inhibition of this protein kinase C in leukemic cells leads to normalization of the investigated lipid release. The data obtained suggests disorders of early membrane-bound reactions in agonist - and a protein kinase C-mediated processes of formation palmitic acid-containing lipid metabolites in the leukemic cells in comparison with the norm.
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7. Romanova S.G., Belickii G.A., Hitrovo I.A., Serebrennikova G.A., Shtil A.A.

Studies of mutagenic activity of positively charged alkyl glycerolipids in ames test.

Mutagenic activity of non-phosphorous cationic alkyl glycerolipid rac-N-{ 4-[(2-Methoxy-3-octadecyloxy)propyl]oxycarbonylbutyl}-N,N-dimethyl-N-(2-hydroxyethyl) ammonium iodide was evaluated. According performed Ames assay results indicated on non-mutagenic properties tested compound. Resulting data open the possibility to carry out biological study in vivo for class of ether cationic glycerolipids and further applications as a potential agent of anticancer therapy.
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8. Pivovarova E.N., Dushkin M.I., Perepechaeva M.L., Kobzev V.F., Trufakin V.A., Markel A.L.

All signs of metabolic syndrome in the hypertensive ISIAH rats are associated with increased activity of transcription factors PPAR, LXR, PXR, and CAR in the liver.

It is known that the metabolic syndrome (MS), which includes hypertension, dislipidemia, glucose intolerance, and obesity leads to cardiovascular diseases. The MS risk is growing catastrophically. Molecular mechanisms allowing to understand the reason of integrated dysfunctions, taking place at MS cases, have remained almost unstudied. The chronical stress plays a crucial role in MS development; therefore in the present work a hypertensive rat strain with Inherited Stress-Induced Arterial Hypertension (ISIAH) was used as a model. It was shown that ISIAH rat strain as compared with the control WAG rat strain is characterized by increased content of triglyceride, VLDL and LDL cholesterols, a decreased content of HDL cholesterol, a high level of apolipoprotein B-100, and decreased level of apolipoprotein Đ•-I. The ISIAH rats body weight was higher as compared with WAG rats; ISIAH rats blood glucose content was higher too. Thus, strain hypertension for ISIAH rat is accompanied by dislipidemia, increased glucose content, and increased body weight, representing a whole set of MS signs. Since at MS cases the systemic abnormalities in lipid and carbohydrate metabolism take place, the functional activity of transcription factors (TFs) participating in integral regulation of lipid and carbohydrate metabolism genes in liver was measured. PPAR, LXR, PXR, CAR DNA-binding activity was increased in ISIAH rats, suggesting involvement of these TFs in MS development. Integrated investigation of PPAR, LXR, PXR, CAR regulatory mechanisms, signal transduction and transcriptional targets will provide insights into the pathogenesis of MS and offer valuable information for designing of drugs for MS treatment.
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9. Berdyshev A.G., Gulaya N.M., Chumak A.A., Kindruk N.L.

Effect of N-stearoylethanolamine on free amino acid levels in rat plasma and liver with burn.

The effect of the endocannabinoid congener N-stearoylethanolamine (NSE) on the content of plasma and liver free amino acids in burned rats was studied. The animals after the thermal burn of the skin received per os during 7 days the water suspension of NSE in the doze 10 mg/kg of body weight. In the other group of rats the suspension was applied on the wound (the concentration of NSE was 10 mg/ml). In experimental animals the total amount of free amino acids in plasma decreased after burn while the total amount of free amino acids in liver significantly increased. In burn animals the ratio of plasma and liver Phe/Tyr and Gly/Val was found to be augmented while the Fischer ratio (Ile+Leu+Val/Phe+Tyr) diminished compared with intact rats. It was shown for the first time that NSE caused normalization of the concentration of some free amino acids and of Phe/Tyr, Gly/Val ratios, and the Fischer ratio in blood plasma and liver of rats with the burn injury.Altogether, these data demonstrate that NSE possesses adaptogenic properties, and is involved in the organism response to a burn. These findings suggest possibility of NSE usage for burn treatment.

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10. Zakaryan A.V., Kazaryan G.S., Zakaryan G.V., Melkonyan M.M., Hovsepyan L.M.

Study of cytokines content and gangliosides metabolism at experimental brain edema.

The content of cytokines, and gangliosides metabolism, and the quantity of lipid peroxidation products were studied at experimental brain edema. Data obtained show increase the level of proinflammatory cytokins and decrease the level of antiinflammatory cytokines during development of brain edema. Along with this we reveal the accumulation of lipid peroxidation products (diene conjugates, hydroperoxides, and malonic dialdehyde). Each fraction of gangliosides decreased, but the product of their hydrolytic dissociation sphingosine increased at experimental brain edema.

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11. Pustovalova R.A., Petrova M.B.

Neopterin as a rarameter, reflecting the inflammatory phase of a dermal wound process.

Effectiveness of the influence of a natural cytokine complex "Superlymph" on a wound process was evaluated in albino rats. The preparation was used right after surgical treatment and then during 5 days. Interrelationship between morphological and immunobiochemical factors on local and organismic levels was studied. During uncomplicated wound process no statistically significant difference in concentration of blood serum neopterin was found. The main changes occured locally. There was correlation between morphological and immunobiochemical factors.

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12. Elizarov A.Yu., Ershov T.D., Levshankov A.I.

Mass-spectrometric investigation of degradation of the inhalation anesthetic sevoflurane in flow anesthesia.

The highest concentration of the Sevoflurane degradation product in the gas mixture was 65 ppm. Biochemical analysis did not reveal any nephro- and hepatotoxic effect

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