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BOOK OF ABSTRACTS

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BIO-ENGINEERING AND REGENERATIVE MEDICINE

TECHNOLOGY OF MICROCONTACT PRINTING FOR DETECTION ABNORMAL PRION PROTEIN (PRP_{27-30}) IN BIOLOGICAL SPECIMENS

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Microcontact printing is a power tool for patterning molecules (etc. proteins) on solid surfaces. This process has ability to create planar sensor coatings with dimensions ranging from tens of micrometers to hundreds of nanometers. Here, we described this method for detection and identification of the abnormal pathological prion protein (PrP_{27-30}).

Materials and methods. The clinical material (blood) was studied in 46 patients (61-89 years) with neurodegenerative disorders. Autopsy samples of human brain tissues (n = 5), who died with clinically diagnosis of Creutzfeldt-Jakob disease (CJD), also were subjected for analysis.

Acquisition of sensory coatings and detection PrP_{27-30}. This method included the following procedures: preparing the master, creating the PDMS stamp, inking the specific anti-prion antibodies on stamp, specific processing of biological samples for the isolation of prion protein and purification of the obtained fraction with proteinase k. The atomic force microscopy (AFM) images of the sample surface were obtained in air in tapping mode, using a Nanoscope IIIa microscope (Bruker, USA), equipped with a J-scanner.

Results. The stages of sample preparation of clinical material have been optimized, the technique of obtaining activated sensory surfaces for controlled adsorption of specific anti-prion antibodies has been unified. With the use of AFM, the tactic of indication of prion protein (PrP27-30) were standardized.

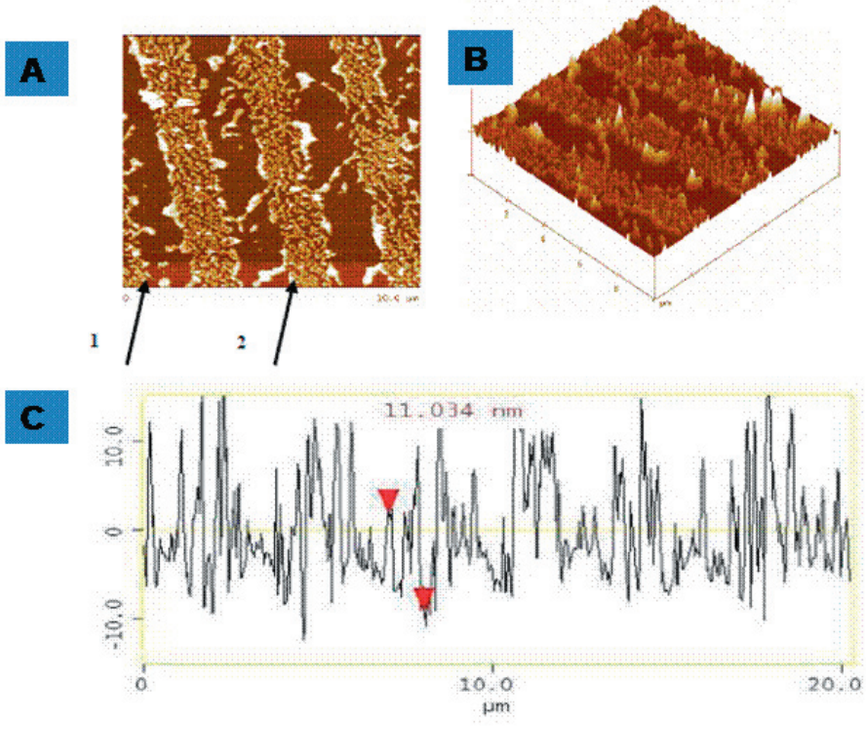

Figure. AFM image of spatial forms of a positive sample on a locally activated silicon substrate after immobilization of positive Prp_{27-30} sample, enzymatic treatment and the stage of treatment with anti-PrP monoclonal antibodies: 1 — bovine serum albumin; 2 — immune complex PrP27-30 + anti-PrP monoclonal antibody: a — AFM in the tapping mode; B — three-dimensional image; C — graphical microprofile of surface

Using AFM, the possibility of identifying and analyzing the fine nanostructural organization of different-dimensional pathological protein components PrP27-30 protein, has been demonstrated. The obtained results are relevant for improving and differentiating neurodegenerative disorders of different genesis.

THE ROLE OF MICROORGANISM ASSOCIATIONS IN THE ETIOLOGY OF INFECTIONS COMLICATIONS OF PRIMARY KNEE ENDOPROSTHESIS REPLACEMENT

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The research investigated the importance of microorganism associations in the etiology of peri-implant infection and the specifics of antibiotic resistance in mixed infections. We retrospectively reviewed the microbiological findings in samples from 75 patients with infectious inflammatory complications of primary knee replacement. The microorganisms were identified on BD BBL™ Crystal™ AutoReader.

Polyetiologic implant-associated complications amounted to 36.8-43.1% of all bacteria verified cases and were represented with a great variety of microorganisms (over 30 species and various associate combinations). We registered the dominance of 2-component associations — 21.8% of all cases, and 7.1% were made up of 4-6-component associations. The associativity coefficient that describes the involvement of every microorganism species within an association was 35.4-42.7% for *S.aureus* strains and 28.1-37.4% for *S.epidermidis* strains suggesting mild involvement in associations and etiological significance in the forms of both monocultures and associates. High associativity coefficient (49.5-62.8%) was attributed to nonfermentable gram-negative *Acinetobacter* bacteria as well as yeast-like *Candida* fungi 71.2-84.5%. The coefficient was 100% for *Proteus spp.* and *Klebsiella spp.* strains.

The number of clinically significant pathogens — MRSA, MRSE, polyresistant enterobacteria, and nonfermentable gram-negative bacteria was statistically ($p<0.001$) higher for associates as compared to monocultures.

Microbiological monitoring of the polyetiology implant-associated infections is a must for diagnostics optimization and adequate casual therapy for this pathology.

PROTEOMIC ANALYSIS AND FLOW CYTOFLUOROMETRY FOR THE ASSESSMENT OF SYSTEMIC INFLAMMATION DESTRUCTIVE PROCESSES IN PATIENTS WITH EARLY SIGNS OF PRIMARY KNEE OSTEOARTHROSIS

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Osteoarthrosis (OA) is the most common degenerative-destructive joint disease in the world.

The research objective was the assessment of systemic inflammation destructive processes in patients with early signs of primary knee OA using flow cytofluorometry and proteomic analysis.

We examined 35 patients with early degenerative-destructive changes in knee tissues as well as 13 donors lacking any musculoskeletal pathologies. The investigation included the determination of qualitative/quantitative compositions of the peripheral blood lymphocyte subpopulations through lymphocyte typing with laser flow cytofluorometry. ELISA was also employed to find cartilage oligomeric matrix protein (COMP) and proinflammatory cytokines (IL-1, IL-6, TNF-α). The digital data were statistically processed in Microsoft Excel 2010, Statistica 6.0 software.

The analysis of the results revealed the trend for the decrease in both absolute and relative contents of T-lymphocytes as well as the increase in natural killer content. The rise of proinflammatory cytokines along with COMP augmentation as compared to indicators of donors was registered.

Proteomic analysis and flow cytofluorometry demonstrated systemic inflammation destructive processes in patients with early signs of primary knee OA involving augmentation of COMP and proinflammatory cytokines along with certain changes in qualitative/quantitative compositions of the peripheral blood lymphocyte subpopulations that can trigger autoimmune inflammation and favor further OA progress.

COLLAGEN-COATED POLYCAPROLACTONE NON-WOVEN FIBROUS MATS FOR REGENERATIVE MEDICINE

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Non-woven fibrous materials are widely used as biodegradable scaffolds in tissue engineering of hollow organs, including urethra, trachea, etc. Due to a good processability and mechanical properties, biodegradable synthetic polymers, such as polylactide, polycaprolactone, etc., are widely used for fabrication of fibrous mats. However, hydrophobicity and a lack of specific sites for cell adhesion/growth on polyester-based materials require its surface modification. In a frame of this work we studied a possibility to coat a non-woven fibrous polycaprolactone-based scaffold by collagen type I using preliminary surface activation of the scaffold by plasma treatment. The fibrous non-woven mats were fabricated via electrospinning technology from 30 wt. % polycaprolactone solution in chloroform using ESR100D NanoNC (Korea). The scaffold surface was treated by low-temperature plasma with an aim of CUTE-1MPR (Korea) operating at 40 kHz and 50 W for 60 sec using air as working gas. The fibrous mats were incubated in 0.5 wt. % collagen solution in 3% acetic acid for 2 hrs; the excess of collagen was washed out with distilled water and the scaffold was dried in a dust-free chamber. Scanning electron microscopy showed that initial mat consists of alignment distributed fibers with a mean diameter of 5 μm. The immobilization of collagen led to an increase of the fiber diameter in 1.2-times, which indicates the presence of collagen on the fiber surface. The successful coating deposition was also confirmed using gravimetric analysis and fluorescein microscopy after staining with selective fluorescein dye. This work was supported by the RFBR (№ 18-29-17050).

OPTIMIZATION OF HUMAN UMBILICAL CORD CONNECTIVE TISSUE DECELLULARIZATION PROCEDURE FOR CREATING A TISSUE-ENGINEERED WOUND COVER

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The most important task of tissue engineering is to create in vivo transplants based on biocompatible non-immunogenic matrices that stimulate cell migration, attachment, and functioning. One of the most promising scaffolds is considered to be the native extracellular matrix (ECM). An available source of homologous biomaterial for creating ECM is the umbilical cord.

Wharton jelly has a huge regenerative potential due to the presence of growth factors and cell adhesion molecules. The umbilical cord is phenotypically similar to embryonic tissues capable of scarless wound healing.

The decellularization procedure removes cells and nuclei, making the product non-immunogenic. In our study, decellularization was performed using two protocols. Protocol 1: exposure to 0.05% sodium dodecyl sulfate (SDS) solution for 24 hours at RT at 130 rpm. Repeated washing with distilled water, centrifugation 10,000 rpm 10 minutes. Protocol 2: exposure to 0.01 M NaOH solution for 4 hours at RT, 130 rpm. Neutralization with a solution of 0.01 N HCL to pH =7.40. Centrifugation 10,000 rpm 10 minutes.

Quantitative assessment of DNA in the ECM showed that both protocols are highly effective in removing nuclear material and absence of whole DNA molecules after NaOH treatment.

Conclusion: decellularization using NaOH is the optimal method, since it allows for better removal of genetic material, requires less time, and the products of the NaOH neutralization procedure are physiological.

HYBRID CORE/SHELL POLYLACTIDE-BASED MICROPARTICLES

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Biodegradable microparticles are versatile tool for various applications, such as drug-delivery systems with targeted/prolonged release, cell microcarriers or starting material for fabrication of 3D structures via additive technologies. Among a perspective particle structures a core/shell one is one of the most promising. A presence of shell of various natures onto polymeric core could be used as to control a drug release rate as well as to enhance microparticle processability or its surface functionality including bioactivity.

The goal of the present study is to evaluate an effectiveness of nanoparticles of various natures for stabilization of polylactide microparticles in a course of their fabrication through an oil/water Pickering emulsion solvent evaporation technique.

This study examined nanoparticles of various natures, i.e. metallic (Au, Ag, Pt, etc.) or element-organic (Co-/Mn-/Fe-/Gd-based chelates) or inorganic (hydroxyapatite, silica), as emulsifiers in aqueous medium. An effect of nanoparticle nature, its concentration and method of dispersion in aqueous medium on total yield of core/shell microparticles, their size and size distribution, surface morphology was evaluated.

ENGINEERING MODELS AND METHODS FOR CALCULATION ASSESSMENT OF THE FUNCTIONAL AND MECHANICAL CHARACTERISTICS OF ENDOVASCULAR STENTS

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The aim of the study was the development of the methodology of the engineering approach to the assessment of the main functional and mechanical characteristics of intravascular polymer stents. The proposed approach allows identifying general behavior patterns of this type of structure, which is necessary for the analysis and selection of the combination of material and stent design.

Methods. Discussion and substantiation of the list of the main functional and mechanical requirements for intravascular stents was conducted. An engineering mechanical model of stent behavior was developed while its opening and subsequent elastic recoil.

Results. A formula for estimating the value of the recoil was obtained by the methods of strength of materials, which allows moving from the functional requirements for the stent to the requirements for the mechanical properties of the material used and the geometric characteristics of the stent elements. Recoil proved to be proportional to the ratio of the yield stress to the Young's modulus of the stent material and to the square of the ratio of the length of the stent elementary cell stratum to its width.

As for example according to the engineering estimates, the material for the stent with Absorb design should have large ultimate strain: $\delta \approx 20\text{-}50\%$ (to ensure maximum stent development); sufficiently high yield strength: $\sigma_y \geq 30$ MPa (so that the stent does not collapse in the vessel); maximum $E/\sigma_y \geq 50$ (to reduce recoil). An assessment of the suitability of some typical bioresorbable materials according to these criteria was given.

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WHOLE PIG KIDNEY DECELLULARIZATION: MODERN PROSPECTS FOR REGENERATIVE MEDICINE

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The extracellular matrix is part of the tissue microenvironment that regulates cell differentiation and proliferation. This function persists after decellularization. Decellularized bioscaffolds can be used as matrices for tissue engineering, regardless of tissue origin.

We performed decellularization of pig kidneys Danish F1 Hybrid. Peristaltic pump and solutions (SDS, deionized water, Triton X-100, PBS) were used for decellularization. For morphological studies were taken control and decellularized kidney. After fixation hematoxylin-eosin staining, Van Gieson and Masson staining were performed.

After hemotoxylin-eosin staining, it can be seen that in the control kidney the cell nuclei are colored blue, the cytoplasm is purple. In the decellularized kidney, these components are absent, only the intercellular substance is visible in the form of empty purple cells. When stained according to Van Gieson, collagen fibers are pink. It can be seen that after decellularization, only the collagen scaffold remained. When stained according to Masson, only the collagen scaffold in the form of empty cells remained after decellularization.

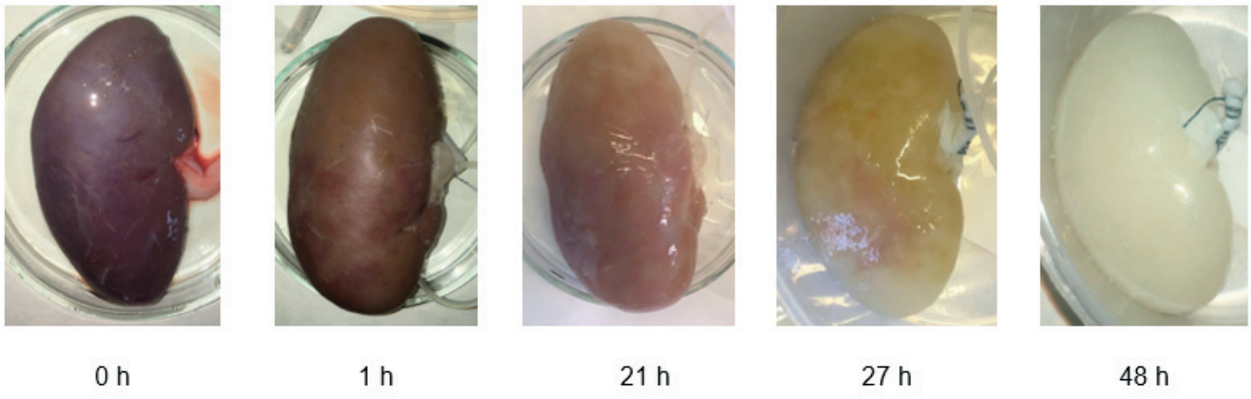

Figure: Pig kidney decellularization progress from 0 to 48 hours

After a multifaceted histological assessment, it can be concluded that the decellularization process was successful: the cells were completely removed, and the intercellular substance remained in place, retaining the structure.

DECELLULARIZATION OF THE WHOLE RAT KIDNEY: TECHNOLOGIES OF THE REGENERATIVE MEDICINE FUTURE

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One of the promising ways of artificial organ creating is decellularization — the removal of all cells from a donor organ using physical and chemical agents. With the subsequent settlement of this intercellular scaffold, it is possible to create a "neoorgan" with correct architectonics and functionality, consisting entirely of recipient's cells.

Decellularization of the Wistar rat kidneys was carried out. For decellularization, a peristaltic pump and solutions were used: SDS, deionized water, Triton X-100, PBS. A control and a decellularized kidney were taken for morphological studies. Hematoxylin-eosin staining, Van Gieson and Masson staining were conducted.

With hemotoxylin-eosin staining it can be seen that in the control kidney the cell nuclei are colored blue, the cytoplasm is purple. The decellularized kidney lacks these components. With Van Gieson staining, it can be seen that after decellularization only the collagen scaffold remained. Masson's staining also showed that after decellularization, only the blue collagen scaffold remained in the form of cells.

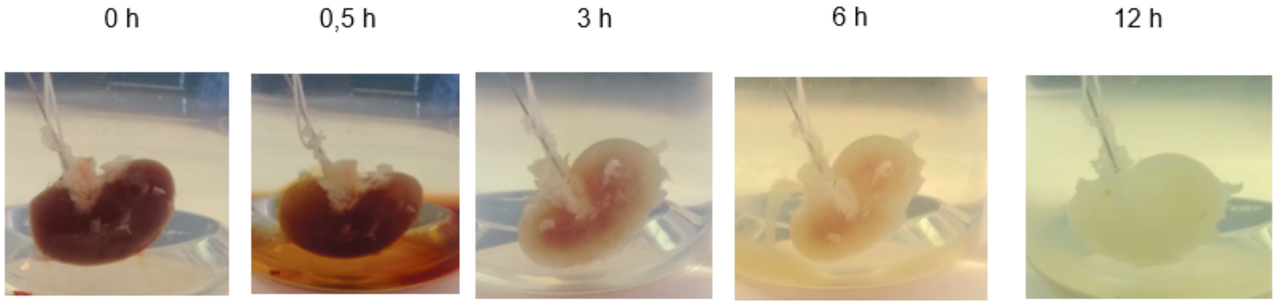

Figure: Progress of rat kidney decellularization from 0 to 12 hours

After a multifaceted histological assessment, it can be concluded that the decellularization process was successful: the cells were completely removed, and the intercellular substance remained in place, retaining the structure.

ANALGESIC BASED ON CROCUS SPECIES FOR USE IN PEDIATRIC DENTISTRY (FORMULATION DEVELOPMENT)

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Due to the increase in the development of allergic reactions in pediatric patients, it is promising to use analgesics based on natural biologically active complexes in pediatric dentistry. It is known that complexes of biologically active substances of plants of the genus Crocus have a proven anesthetic, analgesic, antioxidant, anti-inflammatory effect due to the content of flavonoids, anthocyanins, alkaloids, saponins, and tannins. The pharmacological activity of biologically active complexes of *Crocus sativus L.* (saffron spice) has been studied most fully, which is due to the presence of three main metabolites: crocin, safranal, and picrocrocin. Crocin is the most important glycoside carotenoid. It is acrocetin digentiobiose ester ($C_{20}H_{24}O_4$), with a beta-shaped glycosidic bond able to be hydrolyzed by emulsine (β-glucosidase). Safranal ($C_{10}H_{14}O$) is a cyclical terpenic aldehyde (2,6,6-trimethyl-1,3-cyclohexadien-1-carboxaldehyde). Picrocrocin ($C_6H_{26}O_7$) is a glycoside that due to acids and alkali cracks into a molecule of glucose and into an aglycon named 4-hydroxy-b-cyclocitral. The aglycon loses a molecule of water and easily turns into the volatile compound known as safranal. In independent researches was shown that crocin and safranal suppressed inflammatory pain response as well and decreased the number of neutrophils. We have developed original formulation of analgesic for local use based on stigma and petal alcohol extracts of Iran endemic Crocus species (*C. haussknechtii Boiss. & Reut. ex Boiss*., *C. speciosus M. Bieb.* (Bieberstein's crocus), and *C. sativus L.*). The alcohol extracts can exhibit antinociceptive effects (the action or process of blocking the detection of a painful or injurious stimulus by sensory neurons) in chemically induced pain test as well as anti-inflammatory activity. The developed formulation of analgesic for local use based on stigma and petal alcohol extracts of Iran endemic Crocus species, after appropriate clinical trials, can be recommended for use in pediatric dentistry when performing manipulations accompanied by pain, as well as reducing problems associated with teething in infants.

References

1. Christodoulou E., at al. Saffron: A natural product with potential pharmaceutical applications. Journal of Pharmacy and Pharmacology, 2015: 67 (12):1634-1649.
2. Evaluation of the Effect of Saffron (Crocus Sativus) on Pain Control After Root Canal Therapy in Teeth With Vital Pulps. Kaveh Oloomi, DDS, MS, Zahedan University of Medical Sciences. ClinicalTrials.gov Identifier: NCT01590485. https://clinicaltrials.gov/ct2/show/NCT01590485.
3. Prospective comparative study of extracts on the base of Iran endemic Crocus species for periodontal disease / Fetisova A.N., Mohammad Sheikhjami Karizi // ABSTRACTS BOOK Sechenov International Biomedical Summit 2019, 20.05 — 21.05.2019, Moscow, Russia.M.: Publishing house of Sechenov University, 2019, P. 18-19.

FISH OIL FATTY ACIDS: NATURAL SUPPORT AGAINST COVID-19

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The most common symptoms at the onset of coronavirus disease 2019 (COVID-19) are fever, cough, dyspnea and myalgia, accompanied by leukopenia, lymphopenia, secondary infections and others. The consumption of dietary supplements, such as omega-3 fatty acids, could help improve the treatment and recovery of severe COVID-19 infected patients by reducing inflammatory response and excessive blood coagulation. This hypothesis is based on the well-documented effect of marine omega-3 fatty acids, specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), on inflammation resolution and on their potential for coagulation reduction and arrhythmia improvement. Arachidonic acid (AA) and other unsaturated fatty acids are known to inactivate enveloped viruses and inhibit proliferation of various microbial organisms. However, high dosage of fatty unsaturated acids could increase susceptibility to viruses. For example, replacing AA by EPA and DHA in phospholipid membranes makes the cells prone to oxidative stress when there is an increase in reactive oxygen species concentration in the affected area. It is important to find an appropriate dosage for each patient. Russian market has a wide varieties of fish oil supplements, but options as medical drug are only 2, and their quantity of fatty acids is regulated by Russia State Pharmacopoeia 14. We analyzed samples of fish oil approved in Russia for medical use by gas chromatography with mass-spectrometric detection (GC-MS). The studied samples contained the following fatty acids: 14:0; 15:0; 16:1; 16:0; 18:4, ω-3; 18:2, ω-6; 18:1; 18:5; 18:0; 20:5, ω-3; 20:1; 22:6, ω-3; 22:1. It was detected, that quantity of polyunsaturated fatty acids has range from 24% to 37%, which is sufficient for medical effect. Depends of dosage form, daily dosage is 1 capsule 500 mg or 15 ml of fish oil, which should be safe for organism without adverse events. This administration of unsaturated fatty acids may aid in enhancing resistance and recovery from COVID-19.

References

1. M.M. Rogero, M.de C. Leao, T.M. Santana, Potential benefits and risks of omega-3 fatty acids supplementation to patients with COVID-19, Free Radical Biology and Medicine 156 (2020) 190-199.
2. J.J. DiNicolantonio, J. OKeefe, Importance of maintaining a low omega-6/omega-3 ratio for reducing platelet aggregation, coagulation and thrombosis, Open Hear 6(2019).
3. Undurti N. Das. Can Bioactive Lipids Inactivate Coronavirus (COVID-19)? Arch Med Res. 2020 Apr; 51(3): 282–286.

CREATION OF THE BIO-INK FUNCTIONAL COMPONENT BASED ON A DECELLULARIZED EXTRACELLULAR MATRIX

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Most of the matrix materials used so far for bioprinting cannot form the complex structure of the natural extracellular matrix (ECM) and, thus, they are unable to recreate internal cellular morphology and function.

The aim of the study is to find the optimal composition of bio-ink with decellularized ECM (dECM) for 3D-bioprinting of tissue-engineered constructs for replacing rat cartilage tissue. The choice of cartilage tissue is due to the relative simplicity of structure, which allows us to focus on two main aspects associated with the bio-ink creation: ensuring the scaffold rigidity and the conditions for cell proliferation and differentiation.

Wistar rats were used for the experiment. Costal cartilage was taken from animals. For the first stage of experiment peristaltic pump, detergents and enzymes such as PBS, deionized water, EDTA, SDS, Triton X-100 were used for decellularization. The next step is the lyophilization of the decellularized costal cartilage. This process is necessary for the third stage — homogenization by mechanical grinding in a porcelain mortar. We have obtained cartilage dECM powder, which will be used as a tissue-specific additive to bio-ink to create scaffolds.

This approach is universal: the development of a bioprinting process using tissue-specific bioadditives from dECM can be applied to any tissue. The resulting bio-ink component will promote cell survival, proliferation and differentiation. This bioprinting method should ensure high cell viability and functionality of the printed constructs.

EXTRACELLULAR MATRIX PRODUCTION: DECELLULARIZATION OF THE RAT DIAPHRAGM

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Various alternatives to organ transplantation are currently being explored. One of these methods is the decellularization of organs and tissues. Different methods are used in order to obtain a non-immunogenic, effective and safe scaffold based on the natural extracellular matrix.

Decellularization of Wistar rat diaphragms was carried out. For The decellularization process were used bioreactor and peristaltic pump. Solutions were used: sodium deoxycholate, deionized water, EDTA, PBS. Three types of tissue were taken for morphological examination: control; decellularized; and the diaphragm in PBS solution, which was in the same conditions throughout the decellularization process as the decellularized diaphragm. Hematoxylin-eosin staining, Van Gieson and Masson staining were conducted.

Stainings showed that cells are present in the control kidney, their internal content of nuclei and distributed chromatin are visible. The structure of myofibrillar cells with striated striation is observed. Connective tissue sheath with visible presence of cells on both sides. In the decellularized kidney, these components are absent, only the collagen scaffold remains.

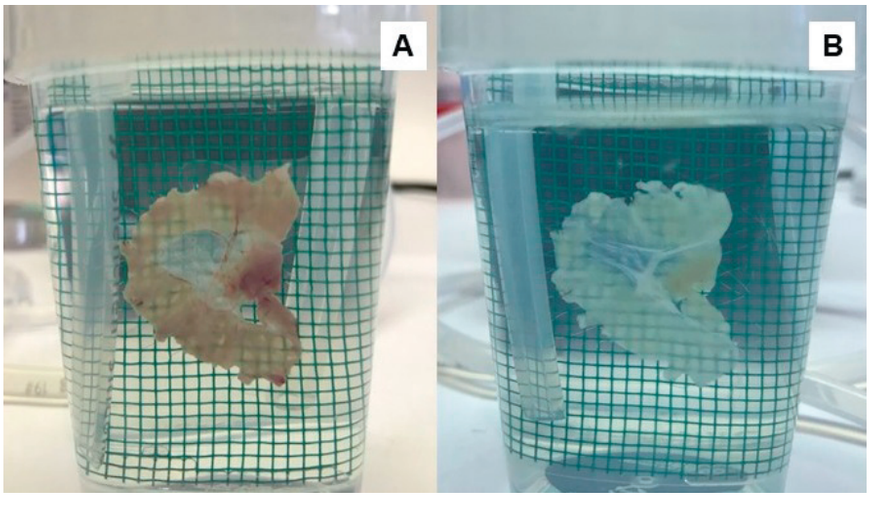

Figure: A — rat diaphragm before decellularization in standard 120 ml beakers for biological samples, B — rat diaphragm after decellularization

Multilateral morphological analysis confirms the success of the process of decellularization of rat diaphragms. The structure of the resulting extracellular matrix is completely preserved, with a complete absence of cellular content.

IG A, M, G SERUM LEVELS AND INDICATORS OF MACROPHAGE RESPONSE IN PATIENTS WITH ENDOPROSTHESIS LOOSENING AFTER *PRIMARY KNEE ARTHROPLASTY*

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Objective. To study the serum levels of Ig A, M, G, MIF, MSP in patients with endoprosthesis loosening after *primary knee arthroplasty*.

Material and methods. We examined 47 patients with implant-associated inflammation (main group); 43 patients with aseptic knee loosening (comparison group), and 20 healthy individuals (control group). Ig A, M, G serum levels were determined with *immunoturbidimetric* method and MIF, MSP with ELISA in patients before the surgeries as

well as in 1 and 12 month of them; in the controls these indicators were determined unitary. The statistical analysis was performed with Mann-Whitney U-test and Wilcoxon signed-rank test.

Results. Ig A increased 1.33-fold in 1 month and 1.67-fold in 12 months in the main group as compared to the controls. Ig M decreased 1.23-fold in 1 month and 1.39-fold in 12 months. Ig G decreased 1.14-fold in 1 month and 1.23-fold in 12 months. MIF increased 2.39-fold in 1 month and 3.60-fold in 12 months of the surgeries. MSP increased 1.11-fold in 1 month, 1.18-fold in 12 months of the surgeries as compared to the controls.

Conclusion. Oppositely directed changes in serum Ig A, M, G classes as well as the increase of MIF, MSP may be of concern in the progress of endoprosthesis loosening after *primary knee arthroplasty.*

NUCLEIC MAGNETIC RESONANCE AND PROTEOME ANALYSIS FOR THE ASSESSMENT OF ARTICULAR HYALINE CARTILAGE TYPE II COLLAGEN IN EARLY SIGNS OF KNEE OSTEOARTHROSIS

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The examination of 36 patients of both sexes aged 38-50 years with 0-I stages of primary osteoarthrosis (OA) included the assessment of urinary type II collagen fragments 24-h extraction (Urine CartiLaps® (CTX-II) EIA assay), T2 Relax mapping, T2-relaxometry of the articular cartilages in 1.5T Hitachi Echelon CT scanner. CT scans were taken in axial and sagittal planes and processed with the software graph editor. We chose ROIs in the articular cartilage plane of medial femoral condyles corresponding to areas with various biomechanical loading to run quantification of T2-relaxometry time.

The statistical analysis of the results with the Mann-Whitney U-test revealed a significant augmentation ($p<0.05$) of urinary type II collagen fragments 24-h extraction — 4.21 (3.05; 8.19) μg/day compared to the control values — 2.20 (1.08; 3.44) μg/day. Under Spearman's coefficient ($R=0.6$) the amount of type II collagen extraction per day correlated ($p<0.05$) to the difference of T2-relaxometry value found between ROIs of the loaded and intact areas of articular cartilage constituting 10 to 17 percent on average.

Conclusion: The specifics of metabolism and structural distribution of type II collagen in articular cartilage in early signs of primary OA are associated with the augmentation of 24-h urinary extraction of its degradation products as well as the increase of its anisotropy on T2-relaxometry evidence.

HYPOXIC MILIEU MODULATES MSC-MEDIATED IMMUNOSUPPRESSION

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Multipotent mesenchymal stromal cells (MSCs) are highly demanded in regenerative medicine and biotechnology due to their high proliferative and paracrine activity, immunomodulation, and low immunogenicity. Previously, we showed that MSCs *in vitro* are strongly regulated by low O_2 (5%) characterizing their tissue niches. Considering the scanty literature data on the MSCs immunosuppression at low O_2, the study of the issue is of special interest.

Here we used human adipose-derived MSCs and mononuclears (PBMCs) from the peripheral blood of healthy volunteers. Phytohemagglutinin-activated PBMCs were co-cultivated with MSCs for 72 hours at 20% and 5% O_2.

During interaction with PBMCs, low O_2 stimulated MSC antiproliferative effect and anti-inflammatory shift of the cytokine profile (lowered production of TNF-alpha, IL-8, IL-6, elevated IL-10 and IDO). The more pronounced effect of direct contact could be related with significant elevation of galectins 1, 3, and TLR4 expression on MSCs at 5% O_2. Genome-wide analysis revealed significant changes in the transcription profile of lymphocytes and MSCs after interaction. Further qPCR analysis showed that low O_2 increased the transcriptional activity of *FOXP3*, *IL10*, *TGFB1*, and *PDCD1* in lymphocytes, as well as *GAL1* and *GAL3* in MSCs.

Thus, low O_2 enhances immunosuppressive properties of MSCs during the interaction with immune cells affecting the functional and transcriptional activity of both cell types. The data obtained are of significant importance for the development of protocols for regenerative medicine and cell therapy.

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EVALUATION OF THE REPARATIVE EFFECT OF FIVE SCAFFOLDS IN A MODEL OF OSTEOCHONDRAL DEFECT OF ARTICULAR CARTILAGE IN RATS

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Background: Articular cartilage is a highly organized tissue that has a limited ability to heal without surgery. Tissue engineering is actively involved in joint tissue reconstruction, which is critical in the progressive stages of articular cartilage degeneration, such as trauma, arthrosis, rheumatoid arthritis, and osteoarthritis. However, the optimal scaffolds for cartilage repair are not yet identified.

Methods: A osteochondral defect was formed on adult Wistar rats using a hand-held cutter with a diameter of 2.5 mm and a depth of up to the subchondral bone. Collagen membranes based on type I and II collagen, decellularized cartilage, a cellulose-based implant (made at Sechenov University) and a Chondro-Gide ® collagen membrane (Switzerland) were implanted in the area of the defect. Visual evaluation was performed using histological sections stained with hematoxylin/eosin, Safranin O/Fast Green, and Picrosirius Red at two time points (2 and 4 months).

Results: Among compared scaffolds, the congruence of the articular surface was most fully restored by decellularized cartilage and collagen type II-based scaffold. The most vivid restoration was observed 4 months after the operation. Formation of hyaline cartilage at the site of the defect was not detected in any of the groups.

Conclusions: Complete replacement of the osteochondral defect occurred when using a collagen membrane based on type II collagen (follow-up period: 4 months), as well as an implant made of decellularized cartilage (follow-up period: 2 and 4 months) however for restoration of hyaline cartilage these scaffolds need to be combined either with cellular therapy or chondro-promoting cytokines.

THE USE OF COLLAGEN WITH HIGH-CONCENTRATION FOR BIOFABRICATION OF CHONDROCYTE-LADEN SCAFFOLD VIA 3D-BIOPRINTING FOR CARTILAGE RESTORATION

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The cells used were obtained from the xiphoid cartilage of two outbred white male rats (the 2nd passage). Bio-ink was based on sterile pig atelocollagen, type I (80 mg/ml). The final cell concentration was $20 \cdot 10^6$ ml^{-1}. The printing was carried out on Rokit Invivo 3D-bioprinter. After the printing, scaffolds were cultured in DMEM with 10% fetal calf serum and growth factors for 4 weeks. Part of the scaffolds was implanted under the skin at the withers of outbred white rats on the day of printing.

One hour after the printing, the cells were concentrated mostly at air bubbles inside the structure and near the outer surfaces of the scaffolds. After two weeks, most of the cells died. After 4 weeks, individual living cells were preserved. According to pathomorphological studies in animals 2 weeks after implantation, a picture of granulomatous inflammation with the destruction of the organic matrix was observed. After 6 weeks, connective tissue was formed under the epidermis, in which, next to the blood vessels, mononuclear macrophages and groups of cells were found. According to morphological criteria, these cells correspond to young chondrocytes.

Scaffold based on high concentration collagen (4%) has the main properties of tissue-engineered structures with collagen content of 0.5-2% in terms of mild inflammatory reactions, rapid degradation and surpasses standard formulations in terms of print quality. The main disadvantage is the low intrinsic porosity of the gel, which prevents the access of oxygen and nutrients, which ultimately leads to the death of most incorporated cells.

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BIOPOLYMERS AS EMULSIFIERS FOR FABRICATION OF POLYESTER MICROPARTICLES VIA OIL/WATER SOLVENT EVAPORATION TECHNIQUE

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Biodegradable microparticles have a great potential as multifunctional cell microcarriers, which could serve as micro-scaffolds for simultaneous delivery of cells/drugs and providing a temporary support for cell adhesion/growth. One of the most simple and flexible method of microparticle fabrication, which allows to control their structure/properties, is an oil/water emulsion solvent evaporation technique. This method requires application of emulsifier to stabilize an oil/water interface. This work aimed to explore a variety of polysaccharides and proteins as an alternative to synthetic emulsifiers. It allows to avoid application of synthetic non-biodegradable components and to enrich the surface of the formed microparticles with bioactive fragments and to widen their functionality. Thus, a variety of biopolymers (proteins, polysaccharides) in a form of macromolecular solutions or nanoparticles were screened in terms of ability to serve as emulsifiers in aqueous phase during fabrication of polylactide microparticles as well as their effect on the microparticle total yield, mean size, size distribution and morphology.

MULTICOMPONENT NON-WOVEN MATS: ELECTROSPINNING VS.ELECTRODE-ASSISTED SOLUTION BLOWING SPINNINGTECHNOLOGY

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Fibrous non-woven matsare promising form of polymeric scaffolds for tissue engineering and being them should meet a wide range of criteria for successful application. The main criteria, i.e. morphology, biocompatibility, degree of biodegradation, mechanical properties, etc., strongly depend on polymer chemical structure andprocessing technology.The work was aiming at fabrication and study of non-woven mats fabricated via electrospinning or (electrode-assisted) solution blowing spinning technology from multicomponent copolymer-containing system (MCS) comprising advantages of synthetic (oligo-/polylactide, polycaprolactone) and natural (gelatin, chitosan) polymers.The multicomponent system was synthesized via mechanochemical approach and due to graft-copolymer fraction synthesis could form stable ultra-fine dispersions in various solvents (i.e. chlorinated ones, hexafluoroisopropanol (HFI), etc.). It allows to fabricate multicomponent materials using a variety of scaffold's processing methods in one step.

The MCS was tested in terms of processability of non-woven mats via a variety of methods, such as electrospinning (ES), solution blowing spinning technology (SBS) and electrode-assisted one (EA-SBS), which lead to formation of either mono— or multifilament fibers. ES allows to fabricate MCS defect-free mats using either chloroform or HFI for casting solution, while traditional SBS wasn't able to provide a structured material. However, EA-SBS was successful in terms of fabrication of mats using HFI, while the usage of MCS solution in chloroform led to formation ofdefects material.

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EFFICIENCY OF USING SUPERCRITICAL CARBON DIOXIDE FOR DECELLULARIZATION OF ARTICULAR CARTILAGE

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The most promising for creating tissue engineering constructs are scaffolds from decellularized tissues due to their potential ability to selectively support the adhesion and proliferation of tissue-specific cells.

Aim. Researching the possibility of achieving complete decellularization of porcine articular cartilage by sequential treatment with surfactants and supercritical carbon dioxide (sc-CO_2).

Materials and methods. The cartilage particles (CP) with a size of 30-100 μm were obtained by micronization with CryoMill (Retch GmBH, Germany). For decellularization sodium dodecyl sulfate and Triton X-100 were used. The treatment of CP with sc-CO_2 was performed with Speed SFE (Applied Separations, USA). The morphology of scaffold was assessed by histological methods. The efficiency of decellularization of CP was assessed using DAPI. The cytotoxicity of the samples was determined by use of human adipose-derived mesenchymal stem cells (hADSCs).

Results. It was found that for complete decellularization the effect of sc-CO_2 must be carried out after surfactant treatment. The combination of actions, including treatment of CP with surfactant solutions, and then sc-CO_2 with the addition of ethanol as a polarity modifier for 8 hours, is optimal for complete decellularization and preservation of the extracellular matrix structure. Active proliferation of hADSCs in the presence of tissue-specific scaffold reveals an opportunity of its use as a cell carrier for cartilage tissue engineering.

Conclusion. The efficiency of using sc-CO_2 to achieve complete decellularization of porcine articular cartilage with preservation of the structure has been shown.

LOCAL PHARMACOLOGICAL ACTIVATION OF HEDGEHOG PATHWAY PROMOTES ONE LEG OVERGROWTH VIA STEM CELL REGULATION

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We have recently shown that longitudinal bone growth is fueled by a stem cell niche, which forms in the growth plate upon development of the secondary ossification centers (SOCs). These SOCs provides a Sonic Hedgehog (SHH) signal to the growth plate, which likely support the stem cell renewal within the niche. However, it is not known if this mechanism can be employed for therapeutic purposes.

To address this, we have placed agarose beads containing hedgehog pathway activator (SAG) right above the growth plate, into the SOC. Thirty-day-old rats were used and SAG-containing beads implanted only into distal femoral SOC. Lateral leg was implanted DMSO-containing beads (control).

The length of the leg with SAG exceeded the other leg by 1.8±0.9 mm 55 days after the implantation. The most noticeable change was observed in the femur length (1.1±0.6, p=0.043), although a weak effect was also present in the tibia (0.5±0.2, p=0.043), suggesting diffusion of the SAG into the adjusted bone. Short-term analysis revealed increased proliferation in the area of the stem cell niche (3.4±2.7%, p=0.043, of Ki67-positive cells 7 days after implantation).

Thus, we have shown that activation of the HH pathway can be achieved locally, promote proliferation within the stem cell niche and cause bone elongation. These experiments provide a proof-of-principle evidences that manipulation of stem cells in vivo can achieve a functional outcome and can be used for therapeutic correction of the limbs growth disorders such as leg length differences.

PECULIARITIES OF DIFFERENTIAL EXPRESSION OF MATRISOME GENES IN MSCS PERMANENTLY CULTURED AT 5% AND 20% O_2

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Local microenvironment factors, primarily the O_2 level, determine secretory activity of mesenchymal stromal cells (MSCs), including extracellular matrix (ECM) production.

Using the Human Ref-8,-12 arrays (Illumina, USA), a whole-genome analysis of the differential expression of ECM genes and regulating molecules in MSCs from adipose tissue of three donors (D1, D2, D3), permanently cultivated at 5% and 20% O_2, was carried out.

Though the number of differentially expressed genes varied: D1 — 98, D2 — 23, D3 — 42, the ratio of core matrisome and matrisome-associated genes was similar about 2:3. Using the HypoxiaDB, in D1-MSCs — 25, D2-MSCs — 23, in D3-MSCs — 16 genes were hypoxia-dependent. Among all 163 genes with altered expression, only 8 were changed concomitantly in three samples and 15 — in two. Among those 8 genes there were glycoproteins — *COMP, ELN, MFAP4, PSG4*, regulator — *LOXL4*, ECM-affiliated *ITGA11*, secreted factors — *CXCL12, PDGFRL*. The expression of *COMP, ELN, ITGA* unidirectionally decreased and *CXCL12, PDGFRL* increased. Among the 15 genes, 9 (*COL6A2, COL6A3, FBLN1, SPON1, PLAU, PCOLCE, SERPINF1, PDGFRA, TGFBP3*) genes were up-regulated and 2 (*EPDR1, IGFBP7*) genes — down-regulated.

Commonly changed genes could be assumed to be most probable ECM molecular targets and allow to predict MSC behavior and ECM composition at “physiological hypoxia” in vitro.

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EFFECTS OF FETAL BOVINE SERUM ON THE PHYSICOCHEMICAL PROPERTIES OF ETOPOSIDE LOADED PLGA NANOPARTICLES

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Etoposide is active in the treatment of a variety of human cancers. Etoposide loaded PLGA nanoparticles as drug delivery systems have advantages over free etoposide since they maximize therapeutic effects and minimize adverse reactions of drug. In bloodstream adsorption of plasma proteins on the nanoparticle surface could lead to physicochemical changes in the formulation, may affect the interaction of nanoparticles with the bio-target.

The goal of this work was to study protein adsorption on the nanoparticle surface and physicochemical characterizations of nanoparticles after different incubation times with fetal bovine serum (FBS) and saline solution.

We have prepared etoposide loaded PLGA nanoparticles (NPs). NPs and 10% or 90% FBS or saline solution were mixed and placed in an incubator at 37 °C. The experiment lasted for 4 hours. Z-potential (surface charge), nanoparticle size, polydispersity index (PDI) were measured using a Malvern ZetaSizer Nano ZS. Protein content was determined by the Bicinchoninic Acid Kit for Protein Determination.

After incubation of NPs with FBS content proteins in FBS solution decreased by 20%. The greatest increase of NPs size and PDI values was obtained with 90% concentration FBS. All the obtained NPs samples were characterized by a weakly negative zeta potential. Incubation of NPs with saline solution did not affect physicochemical characterizations of NPs. The results indicate that FBS proteins adsorb on the nanoparticle surface and increase of NPs size and PDI values.

HEPATOPROTECTIVE ACTIVITY OF THE SILYBIN-LOADED POLYMERIC NANOPARTICLES

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Silybin is used for the treatment of liver dysfunctions of various etiologies. The low effectiveness of silybin is explained by its low solubility and bioavailability. A highly effective strategy for increasing solubility and bioavailability is the incorporation of silybin into a polymer carrier.

The goal of this work was to study hepatoprotective activity of the silybin-loaded polymeric nanoparticles (SLNs) compared with the substance of silybin. SLNs with an average particle size of 200 nm were prepared by the single emulsion method. The silybin content was 5%. The hepatoprotective effect was studied in C57bl/6 mice using a model of acute toxic hepatitis caused by carbon tetrachloride (CCl_4). Mice were treated with SLNs in a dose of 100 mg/kg prior to CCl_4 injection. The animals were euthanized and blood samples were taken to determine the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP).

SLNs reduced the toxic liver damage to a greater extent than silybin. The activity levels of ALT, AST and ALP were 25%, 11% and 43% lower in the group of mice treated SLNs compared with mice after CCl_4 injection without treatment. The cytolytic and cholestatic syndromes were reduced. Aminotransferases activity in mice treated with silybin was similar to the activity of ALT and AST in mice after CCl_4 injection, but ALP activity was lower by 12%. The results indicate the polymer carrier capable to enhance hepatoprotective activity of silybin that may be associated with increased bioavailability.

FIBRIN GEL AS A FUNCTIONAL BIOINK FOR 3D BIOPRINTING

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The 3D bioprinting is an emerging technology with different applications in treating people who require restoration of injured or completely lost organs and tissues. This method is rapidly evolving that combines multiple cell types, biomaterials, and bioactive molecules in a patterned model to mimic the complexity and the structure of the real human tissue.

Bioinks are one of the key elements of bioprinting, and the fundamental possibility of creating tissue constructs depends on its properties. To date, there is a growing number of studies trying to develop a "perfect" bioink, but this goal remains not to be reached. Thus, our research aims to develop functional fibrin-based bioink for the generation of three-dimensional (3D) tissue products with structural organization.

Modified fibrin was cross-linked and stabilized due to exposure of PEGylated fibrinogen to thrombin to form the final shape and architecture of the designed construct. Using a mixer, the gel and cell suspension were mixed (3T3 cell line — mouse fibroblasts). The prepared optimal cell-laden bioink formulation was tested on a BioX extrusion bioprinter (Cellink, USA). The formed constructs were cultivated in the complete nutrient medium and incubated for 7 days at 5% CO2. Cell viability was evaluated using Live / Dead staining and standard colorimetric tests (MTT, LDH, Alamar Blue). Cell proliferative activity was determined using the PicoGreen test. The viscosity was determined by a laser viscometer (EMS, South Korea).

As a result of our research, we have optimized the component composition of bioink and achieved a viscosity that ensures good printability. The optimal ratio of the components combination in the blend provided the high printing quality which enabled proper cell maturation and phenotypic development.

The cells within the construct remained viable for 7 days and proliferated. They stretched out and formed numerous intercellular contacts.

Thus, the resulting bioink and the constructs printed from them can be a platform for 3D formation of organs and tissues.

THE INFLUENCE OF BIOPOLYMER COLLAGEN-CONTAINING HYDROGEL ON THE SURVIVAL OF ISOLATED HUMAN PANCREATIC ISLETS

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Objective. Due to the action of a number of damaging factors during the isolation and culturing procedure, islets of Langerhans (iL) have the low survival rate and functional activity. The preservation of the structure and function of iL *in vitro* and *in vivo* is facilitated by artificial scaffolds, capable of simulating the biological microenvironment for iL.

The aim. To investigate the viability of human pancreatic islets during co-culturing with biopolymer microheterogeneous collagen-containing hydrogel (BMCH).

Methods. iLwere isolated from the pancreas of posthumous donors using a modification of the classical technique with collagenase. Identification of iL obtained was performed by dithizone staining. iL culturing in monoculture and in the presence of BMCH was carried out under standard conditions.The iL viability was evaluated using the LIVE/DEAD® Cell Viability Kit.

Results. It was discovered that the islets of Langerhans cultured with BMCH for six days turned out to be more viable, retained the integrity and characteristic structure, whereas in the control islets in monoculture, the formation of cavities, signs of fragmentation, and a significant number of dead cells with red fluorescence were observed.

Discussion. Culturing of iL with BMCH which introduces components of the native microenvironment promotes the prolongation of islet viability *in vitro*.

MESENCHYMAL STEM CELL SENESCENCE AND AUTOPHAGY REGULATION

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Mesenchymal stem cells (MSCs) are involved in the physiological renewal and regeneration of tissues. Cell senescence is associated with increased fraction of damaged structures and changed intracellular homeostasis. Elimination of damaged molecules and organelles occurs via autophagy that can be important in the context of aging. Cultivation under low oxygen level can be used as an approach for enhancement of MSC therapeutic properties and “slowing down” cell senescence. The goal of this work was to study morphological and functional characteristics and expression of autophagy-associated genes during replicative senescence of MSCs under different oxygenation.

Long-term cultivated MSCs demonstrated senescence markers. The study revealed changes in the transcriptional regulation of autophagy. Upregulation of autophagosome membrane growth genes (*ATG9A*, *ULK1*), autophagosome maturation genes (*CTSD*, *CLN3*, *GAA*, *GABARAPL1*), autophagy regulation genes (*TP53*, *TGFB1*, *BCL2L1*, *FADD*, *HTT*) was shown. These changes were accompanied by downregulation of *IGF1* and *TGM2* expression. Increase of the lysosomal compartment volume was observed in the senescent MSCs that also indicated increase of their degradation activity. The number of lysosomes was decreased following prolonged cultivation under low oxygen concentration (5%). The replicative senescence of MSCs under conditions of different oxygen levels led to the similar modifications in the expression of the autophagy-associated genes.

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DETERMINATION OF THE CORRECT CONDITIONS FOR THE ANALYSIS OF THE METABOLIC STATUS OF LIVER TISSUE USING MULTIPHOTON MICROSCOPY

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Nowadays fluorescence lifetime imaging microscopy (FLIM) has been extensively applied to study cellular metabolism in the liver. However, there is neither an established approach to analyze the data, nor have appropriate protocols been developed to maintain the optical metabolic characteristics in the *ex vivo* liver tissue sample. We showed that a tri-exponential decay the most correct fitting model for the fluorescence signal from nicotinamide adenine dinucleotide (NAD(P)H) in liver tissue, due to the high synthetic activity of liver cells. Also, we proved that the use of *ex vivo* samples allows the most appropriate processing of the FLIM data.

Finally, we determine the medium that maintains the initial metabolic state of hepatocytes most effectively. Our results should be particularly relevant for the interrogation of liver samples, not only in laboratory research, but also in clinical settings in the future.

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INFLUENCE OF SCAFFOLD STRUCTURAL HETEROGENEITY ON STEM CELL METABOLISM

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A lot of factors that influence on cell behavior and tissue formation when using scaffolds are known. Those factors include the scaffold material, mechanical characteristics, surface roughness, porosity and many others. Here we focused on a different basic parameter affecting the cell behavior — structural heterogeneity. We obtained two types of scaffolds (heterogeneous and homogeneous) by two-photon polymerization technique. The scaffolds were seeded with mesenchymal stem cells (MSC) and studied by the different technologies of optical bioimaging. We analyzed the cell metabolism by multiphoton microscopy and FLIM (Fluorescence-Lifetime Imaging Microscopy). MSC behavior and metabolism were found to have significant differences between the heterogeneous and homogeneous scaffolds. We assessed fluorescence lifetimes of energy cofactors NADH and NAD(P)H for targeted analysis of metabolic pathways occurring in the cells. The level of protein-free and protein bound NAD(P)H for the cells on the heterogeneous and homogeneous scaffolds was varied. A shift to a more intensive process of anaerobic glycolysis occurred in MSCs on homogeneous scaffolds, which possible indicates a poor cell aeration. MSCs on scaffolds with a heterogeneous structure did not undergo significant changes in metabolic status and showed more stable values of all parameters at all time points.

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CREATION OF COMPOSITE BASED ON CARBON NANOTUBES AND ALBUMIN BY FEMTOSECOND LASER RADIATION FOR TISSUE ENGINEERING STRUCTURES

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It is important to control parameters such as temperature and transmission during composite formation from liquid dispersions. Femtosecond laser radiation (repetition rate 80 MHz, pulse duration 140 fs) allows one to reduce the heating temperature of the material in comparison with the effect of continuous laser radiation. This indicates the possibility of reducing the thermal destruction of biological tissue in the case of using this material as a solder. Monitoring material transmission, in turn, makes it possible to determine precisely the moment of the formation of the composite from the liquid dispersion. During this process, a serious change occurs, resulting in a strong darkening in this area. The process itself corresponds to a first-order phase transition. In the temperature range 45-50 ° C, continuous laser radiation forms a composite, with the process-taking place with a pronounced region of the two-phase state, in which the chemical potentials of the components in the phases are equal. In the case of femtosecond radiation, the same processes occurred in the temperature range of 35–45 ° C, while this region becomes less noticeable with increasing power. The process itself is explained by the interaction between the aggregates, which are combined into hierarchically oriented structures. Mainly single-walled carbon nanotubes absorb the used laser radiation with a wavelength of 810 nm and is then energy transferred to albumin. Composites formed by laser radiation have high strength. *In vitro* studies of cell growth in the presence of the composites were carried out by quantitative (MTT test) and qualitative (microscopy) methods. It was found that the number of cells grown on the composites exceeds the number of cells in the control after 72 hours of incubation. The cells on the composites formed a monolayer, their morphology does not differ from the morphology of cells in the control. *In vitro* studies indicate positive effect of the composites on cell adhesion and proliferation and, therefore, on the possibility of their use for tissue regeneration.

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ACTIVATION OF NEUTROPHILS BY THE PERICARDIUM SCAFFOLD

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Coordinated action of different cells at the site of scaffold implantation ensures effective tissue regeneration. Neutrophils are the innate immune cells recruited and activated at the site of tissue damage earlier than the other cells; they largely determine the overall response of the immune system to scaffold implantation. Proteins bound on a scaffold are believed to be responsible for the neutrophil adhesion and activation. We used luminol-dependent chemiluminescence, flow cytometry and confocal microscopy to assess the responses of neutrophils in whole blood and in plasma after the exposure to the scaffold decellularized bovine pericardium (collagen type I) crosslinked with genipin. Incubation of whole blood with the scaffold caused time-dependent activation of blood neutrophils as evidenced by the production of reactive oxygen species (ROS). Addition of the scaffold to the suspension of neutrophils in autologous plasma led to cell adhesion on the scaffold and to a partial shedding of L-selectin from cell surface, but did not cause a substantial increase in ROS production.

This suggests that the respiratory burst of neutrophils in whole blood is due not only to the proteins and neutrophils adsorbed on the material, but also to other blood cells, most likely platelets. Understanding the mechanisms of neutrophil activation by scaffolds is important in the context of developing new approaches for regulation of the immune response.

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RIB PERICHONDRIUM-DERIVED CELLS FOR ARTICULAR CARTILAGE TISSUE ENGINEERING

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Articular cartilage lesions are unable to heal due to the limited intrinsic regenerative capacity of the tissue and leading to joint destruction. However, rib perichondrium has sufficient regenerative potential to restore damaged rib cartilage. According to this fact, we hypothesize that perichondrium could be promising cell source for cartilage regeneration and tissue engineering.

Here we compared the viability, proliferation and spheroid formation of the cells, derived from ovine rib perichondrium and articular cartilage.

We found that both types of cells stay viable under standard culturing conditions during the whole 2D culture period and for 14 days in 3D spheroid culture, formed in agarose microplates (3D Petri Dish, Microtissues®). In 2D monolayer culture, rib perichondrium-derived cells doubled their population two times faster than articular cartilage chondrocytes, which helps harvest more cells and avoid their dedifferentiation.

In 3D culture equivalent diameter of spheroids formed from rib perichondrium-derived cells increased from 488,5 (day 1) μm to 674,8 μm (day 14). Moreover, these spheroids contained a fibrous matrix. Spheroids formed from articular cartilage chondrocytes contained only cells and decreased in their equivalent diameter from 523,5 (day 1) μm to 307,4 μm (day 14). Implanted into the model injury of articular cartilage, both types of spheroids were able to adhere to the wound surface, spread, and merge.

Taken together, our results indicate that rib perichondrium-derived cells have better regenerative potential than articulated cartilage chondrocytes, and, therefore, rib perichondrium could be a new source of cells for articular cartilage regeneration and tissue engineering.

POSSIBILITIES OF REGENERATIVE MEDICINE TECHNOLOGIES IN EXTENSIVE SOFT TISSUES DEFECTS COVERAGE

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The effectiveness of a fetal fibroblasts (FFbl) culture transplantation assessed in 18 burn patients treatment. The control group included 18 burn patients treated without cell technologies. Comparison parameters were: autodermoplasty (ADP) timing; the number of ADP; hospitalization duration; difference in area of wound epithelization. Statistical data processing was carried out using the program Statistica 6.0 for Windows. Differences in study groups were considered statistically significant at $p < 0.05$. FFbl culture transplantation in patients with extensive skin defects was performed on average two weeks (14.88 ± 3.56 days) after a burn injury. The ADP timing in the main and control groups did not differ, not exceeding on average 19.12 ± 2.01 days ($p = 0.48$). On average, the patients underwent 2.71 ± 0.67 surgeries with cell technologies utilization. The use of the FFbl culture to eliminate extensive skin defects in burn patients can reduce the need for ADP by 1.6 times. The latter is possible due to the acceleration of the granulation tissue formation with the active formation of the epidermis within a week. Complete epithelization of burn wounds is possible by 14 days after FFbl culture transplantation. Regenerative medicine technologies are successfully implemented in the treatment of patients with extensive soft tissue defects. The efficiency of FFbl culture transplantation is based on the formation of a substrate in the wound, which can be considered a temporary biological coating, which accelerates the wound healing process phase change from exudative to proliferative. It also prepares wound surfaces for autodermal flap closure.

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RS 6991952 EBF2 POLYMORPHISM IS NOT ASSOCIATED WITH THE DEVELOPMENT OF ANTERIOR ABDOMINAL WALL HERNIAS IN RUSSIAN POPULATION

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In recent years, the role of genetic factors in the formation of predisposition to anterior abdominal wall hernias has been actively studied. In the only genome-wide study of inguinal hernias (Jorgenson E. et al. 2015), conducted in the USA, 4 loci were found most associated with the development of inguinal hernias. The results of this genome-wide study have not been replicated in any of the European populations, incl. and in the Russian population. Moreover, the study did not study the associations of these genes with other subspecies of hernias of the anterior abdominal wall. Previously, we examined 2 (EFEMP1, WT1) of 4 polymorphisms.

Purpose. This study investigated whether rs 6991952 EBF2 single nucleotide polymorphism are associated with anterior abdominal wall hernia in the Russian population.

Materials and methods. DNA samples were obtained from 277 patients with anterior abdominal wall hernia and 263 age-matched healthy controls. Genotyping was performed by TaqMan-based PCR. Detecting of associations between SNPs and hernia risk was performed by logistic regression analysis.

Results. We found that the polymorphism rs 6991952 EBF2 is not associated with risk of hernia

Conclusion. Our study showed for the first time that rs 6991952 EBF2 is not associated with the risk of developing an umbilical, incisional hernia in the Russian population.

ANALYSIS OF TOPOGRAPHY OF SH-GROUPS IN GREY HUMAN HAIR SHAFTS

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Disulfide bonds are essential for hair protein structure and regeneration, being abundant in high molecular weight keratins and low-molecular keratin-associated proteins. They are formed in keratinization zone of hair follicle and further can be photomodified by UV -irradiation, generating thiols among other products [Fedorkova et al 2016]. However, very little is known about hair topography of SH-groups. Terminal 10-cm-long grey hair shafts of two volunteers were cut into proximal (0.3-2 cm from hair root) and distal (8-10 cm from root) segments. Thiol content in soluble proteins was assessed in the segments of 40 hairs by Ellman's method, and 12 hairs were analyzed by Raman microspectroscopy. According to integral Raman intensities of peripheral (underlying hair cuticle) and central (close to medulla) regions of transverse hair cuts, thiol content in proximal segments was slightly higher (by 0.4%) than in the distal ones, in both regions ($p<0.05$). Thiols in soluble proteins also declined from the proximal to distal segments (from 0.78 ± 0.08 to 0.48 ± 0.06 μg/g, $p<0.05$). Intensity of SS-bonds in the central regions grew from the hair roots to tips by 6% while in the peripheral region it decreased by 2.5%. The pronounced reduction in thiol content registered in the low-molecular soluble proteins of distal hair segments could be caused by their partial loss, presumably due to regular aqueous extraction. The increase in SS-bonds in the central region may result from the reactions of thiol exchange in the hair shaft.

OSTEOCOMMITED MSC EXTRACELLULAR MATRIX PRODUCTION AND PROTEASE SECRETION UNDER SIMULATED MICROGRAVITY INFLUENCE

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The extracellular matrix (ECM) determines tissue mechanical properties and deposits growth factors. It is synthesized by bone cells, constantly renewing itself, and its composition depends on a wide range of factors. The reasons for bone tissue properties negative changes in space flight may be in ECM components synthesis violation. The aim of this work was to assess simulated microgravity effect on collagen and non-collagen ECM proteins production.

In this work, we used MSC from adipose tissue, which were cultured under standard conditions using osteogenic inductors. A Random Positioning Machine (Dutch Space, Netherlands), was used to simulate microgravity effects.

After exposure in RPM during 10 days, collagen proteins content decreased by 15% in intact cells. In osteocommited, the decrease was not significant. In both intact and osteocommitted cells, simulated microgravity caused increase non-collagen proteins content. A decrease in the production of collagen by MSCs can provoke a decrease mechanical tensile strength of bone tissue, a weakening of MSCs adhesion to the extracellular matrix, and MAPK signaling inhibition, which is responsible for osteogenic differentiation. In addition, matrix proteases MMP1, MMP3 and cathepsins A, B, D secretion increase was noted in both groups.

Thus, simulated microgravity effects cause changes in ECM proteins production, which may be the reason of negative changes in bone tissue mechanical properties, an osteogenic potential of progenitor cells decrease, and increase of proteolytic processes.

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TRANSLATIONAL AND PERSONALIZED MEDICINE

INTERNATIONAL MEDICAL CLUSTER BIOTECHNOPARK: CORE PROJECT IN RUSSIAN BIOTECHNOLOGY

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The International Medical Cluster is a largest medical infrastructure project in Russia established and run by the Moscow Government. Our Mission: Development and transfer of medical technologies and practices that are demanded by Russian healthcare system and have competitive advantages to export.

The IMC BioTechnopark is a special 125 000 sq.m. area at the International Medical Cluster based in Skolkovo, equipped with medical university and scientific infrastructure to support start-ups, train world-class specialists, develop technologies, and manufacture drugs and equipment.

The IMC Medical Technopark will have legal advantages the Federal Law on the International Medical Cluster No.160-FZ (2015). Translational medicine is the functional core of the technopark.

Key elements of the BioTechnopark are education (EDU), laboratory R&D (LAB) and industrial medical technology (PRO) platforms.

EDU platform will include State and private medical universities interlinked for breakthrough medical technologies for the domestic market with strong export potential.

PRO will be focused on mature biotech projects and technology transfer and export-oriented import substitution. Cyclotron for isotopes production for radiomics and teranostics solutions will be built.

LAB designed for pharmaceutical and medical technology companies working on breakthrough medical technologies for the domestic market with strong export potential.

IMC BioTechnopark should become a unique technological ecosystem that unites various participants for the creation of new medical technologies in the paradigm of translational medicine.

NANOTECHOLOGICAL APPROACH FOR DIAGNOSIS OF THE HEREDITARY RESPIRATORY TRACT DISEASE — *KARTAGENER'S SYNDROME*

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Currently, much attention is paid to the role of the epithelium in the pathogenesis of the respiratory disorders. It should be noted that functional and morphological changes in the ciliary epithelium appear much earlier than clinical manifestations start. These abnormalities can be more accurately identified using high-resolution microscopy techniques, such as atomic force microscopy (AFM).

Objective. To characterize the organization of ciliated epithelial cells and to identify the specific biomarkers of cell cytoarchitectonics in hereditary anomalies of the respiratory tract by using nanoscopic analysis.

Materials and methods. The main group consisted of 25 children (age — 4-17 years) with chronic lung diseases (cystic fibrosis, primary ciliary dyskinesia, bronchiectasis). Taking the biological materials (smears from the tracheal mucosa) was carried out during scheduled bronchoscopy. Topographic images of ciliary epithelium were obtained with a Nanoscope IIId microscope MultiMode (Bruker, USA), equipped with a J-scanner. We used contact cantilevers CSC38/AIBS (spring constant — 0.03-0.09 N/m, resonance frequency — 6-32 kHz) and tapping microprobes NSC15/AlBS (spring constant — 3-48 N / m, resonance frequency — 60-330 kHz).

Results. The AFM analysis made it possible to characterize morphology, surface topography of ciliated epithelial cells, goblet cells and other cellular elements. Also nanoscopic analysis revealed abnormalities in the organization of cilia (figure).

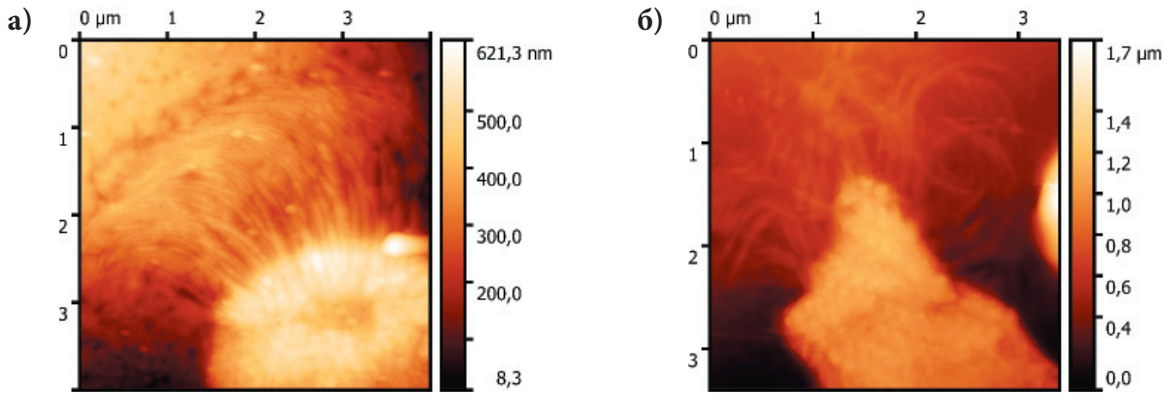

Figure. AFM photographs of the abnormal organization of cilia in 4 patients (b) in comparison with control (a)

It was found that in four children the ciliated epithelium had an unusual morphology. The cilia were located randomly. with a disturbed branching center and resembled the appearance of «twisted rods». In addition, the diameter of these cilia did not match indicators of the norm (~ 200 nm), but varied significantly (from 95 to 160 nm).

Thus the using AFM allows a more informative, accurate and in-depth assessment of the pathomorphosis of ciliated epithelium. The obtained data are relevant for the development and choice of tactics for optimal therapy. This approach makes it possible to efficiently identify some forms of congenital pathology and assess the degree of damage at the subcellular level.

MEDICINAL PLANTS IN TRADITIONAL NANAI MEDICINE

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Traditional intangible values are transfered from generation to generation, from person to person, bypassing institutional forms. They ought to be constantly recreated by the humanity; this way of inheritance makes them especially fragile and vulnerable.

Over the decades, there has been a tendency for the population to decline in Russia. According to the All-Russian Population Census by 2010, the population in the Russian Federation decreased by 2.3 million. inhabitants [9], or almost 2%, compared with 2002 and 4.1 million people, or almost 3%, compared with 1989.

Expensive medicines, unsatisfactory medical care, the transition to paid medicine — all this led to a deterioration in the quality of life, the state of health of the population and an increase in mortality. In connection with the increase in prices for medicines, it becomes necessary to treat the population with accessible natural remedies, making the problem of studying traditional medicine of indigenous small peoples of the North urgent.

For instance.

testimony	plant name in Nanai	plant name
In case of bruises, diseases of the joints, several types of trees are used:	moni cocton	Amur velvet
	piagdan	white birch
	polo	aspen
	khoronkola	Mongolian oak
	unyunkure	wild apple
	chingbora	black birch
	mono	maple
	hotolan	acacia
	burenkule	young ash, 4 years old

Life instilled in the Nanai people a sense of reverence for nature, gave them a rich experience in healing with herbs, roots, and animal products. Traditional healers used plants to treat patients.

DNA METHYLATION-BASED AGE PREDICTION FROM BUCCAL SWAB SAMPLES: THE LEVEL OF METHYLATION OF 6 CPG MARKERS

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Background and Objectives. Buccal epithelium is one of the most common biological samples at the crime scene. Criminalists are interested in the possibility of predicting the age of an unknown person from biological samples left at the crime scene. Chronological age can be determined using CpG markers analysis. For buccal epithelium, such markers in the *KLF14*, *TSSK6*, *SST*, *TBR1*, *SLC12A5*, and *CNGA3* genes.

Purpose. The purpose of the study is to calculate the values of the correlation coefficients (R) and determination (R^2) for CpG markers in the *KLF14*, *TSSK6*, *SST*, *TBR1*, *SLC12A5*, and *CNGA3* genes to prove the chronic age of an unknown individual based on analysis of buccal epithelium samples, as well as assessing the accuracy of predicting chronological age based on a regression model.

Methods. In this study the methylation level of 6 CpG markers for buccal swab samples was analyzed for 82 people of Belarusian nationality using SNaPshot technology — cg14361627 (*KLF1*), cg08928145 (*TSSK6*), cg00481951 (*SST*), cg12757011 (*TBR1*), cg07547549 (*SLC12A5*), cg19671120 (*CNGA3*). We calculated in SPSS v.20.0 software Spearman correlation coefficients using the bootstrap function (1000 samples), 95% confidence interval, the determination coefficients R^2 (and corrected R^2), the median absolute deviation (MAD), the root mean square error (RMSE). Methylation level data were normalized using a non-linear transformation within [0, 1].

Results. The highest calculated R coefficients were obtained for markers cg07547549 (*SLC12A5*), cg14361627 (*KLF14*) and cg12757011 (*TBR1*). When all 6 CpG markers for the «Testing dataset» MAD = 4.69 years (RMSE = 1.39, R^2 = 0.620). As part of the analysis on the impact on the change in the coefficient of determination (R^2), the CpG markers are arranged in the following sequence: cg14361627 (R^2 = 0.581), cg19671120 (+0.099 to the previous value of R^2), cg08928145 (0.053), cg00481951 (0.016), cg07547549 (0.005), cg12757011 (0.001)

Conclusion. Thus, using 6 CpG markers, we can predict chronologic age from samples of buccal epithelium with an accuracy of no worse than 5 years. In the future, we will expand the group of studied samples and reduce the prediction error.

Conflict of interests. The authors declare no conflict of interests.

ROLE OF TRANSMEMBRANE CHLORIDE TRANSPORT IN VASCULAR SMOOTH MUSCLE CONTRACTIONS IN METABOLIC SYNDROME

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Regulation of vascular tone is supported by contractile activity of smooth muscle cells (SMC) located in the walls of blood vessels. Change in SMC contractile responses may occur in various pathological conditions, including metabolic syndrome (MS). Chloride channels (Cl^- channels) and Na+,K+,2Cl— cotransporter (NKCC) are the importance in the development of vascular dysfunction.

The MS model was performed on male Wistar rats (n=23). Rats were separated into control and experimental groups. The rats from the control group were fed standard rat chow. The rats from the experimental group had a high-fat, high-carbohydrate diet for 12 weeks. The contractile activity of the smooth muscle segments of the rat aorta was studied by the mechanographic method.

It was found that upon stimulation of aortic SMC by phenylephrine (10 μM) a decrease in the amplitude of contractions of SMC of the experimental group was occurred. Animals from the experimental group had a decrease in the vasorelaxing effect of acetylcholine, which proves the development of endothelial dysfunction. The pretreatment of the ring segments with niflumic acid, Cl^- channels blocker, bumetanide, an NKCC inhibitor, caused a decrease in the contractile activity of the rat aortic SMC of the experimental group. The data obtained indicate the involvement of transmembrane chloride ion currents in the regulation of vascular smooth muscle contractions in MS.

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POTENTIALS FOR INDIVIDUAL ASSESSMENTS OF MTOR-LINKED PROTEIN PHOSPHORYLATION CASCADES IN PATIENTS WITH AUTISM SPECTRUM DISORDERS

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Since autism is a common phenotypical sign of autistic spectrum disorders (ASD), the neurodevelopmental disorders having very different often unknown background, the search for regularly affected molecular pathways represents a direction to the discovery of individual pharmacological phathogenetically targeted treatments. Among signaling cascades involving protein phosphorylation, mTOR is a central signaling pathway controlling events and processes (including the control of protein synthessis) which are crucial for developing nervous system and neural circuits. Analysis of contemporary literature shows, that substantial deviations of mTOR pathway' activity and defects in mTOR-linked pathways are present in ASD, some of them (syndromic autism) is relatively deeper studied and modeled, other (idiopathic autism) is poorly studied. A great experience of usage of biological markers in line with clinical diagnostic signs in ASD differentiation and diagnostics is accumulated in Russia (Simashkova et al., 2019, Mukaetova-Ladinska et al., 2018). The biological markers include electroencephalography and immunological assessments and tests. Taking into account the heterogeneity of ASD, and regarding the fact that platelets contain many proteins and protein kinases involved in mTOR and mTOR-linked pathways in platelets, the blood platelet studies in patients with ASD, and especially in children with high risk for ASD, as early as possible, seem rather promising biochemical direction to search for prevention of neurodevelopmental anomalities due to enormous activities of mTOR-linked pathways.

Mukaetova-Ladinska EB et al., Zh Nevrol Psikhiatr im S S Korsakova 2018, 118(12):92-99
Simashkova NV et al., J Autism Dev Disord 2019, 49(9):3906-3914

PLATELET GLUTATHIONE METABOLISM ENZYMES IN WOMEN WITH MAJOR DEPRESSION AND LATE ONSET SCHIZOPHRENIA

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The urgency of mental health research in old age is due to general population aging and increase in number of elderly patients with schizophrenia and depression. We focused on determining the activity of platelet glutathione metabolism enzymes in elderly women with depression episode (DE, n=34, 55-81 years old) in recurrent depression or bipolar disorder and late-onset schizophrenia (LOS, n=17, 45-86 years old) and to reveal relationships between activities of these enzymes and clinical features. As compared with control group (women without mental and neurological diseases, n=19, 44-81 years old), significant decrease in activity of platelet glutathione-S-transferase (GST) was revealed in DE or LOS ($p=0.017$ and $p=0.048$, respectively). GST activity in DE or LOS did not significantly change during treatment. GST activity was associated with the age at onset in LOS ($R=-0.502$, $p=0.040$) and in DE ($R=-0.385$, $p=0.035$). In DE, baseline activity of glutathione reductase (GR) was associated with Hamilton Depression Rating Scale total score after the treatment course ($R=-0.440$; $p=0.009$), and baseline GST activity ($R=0.350$; $p=0.043$) was associated with Hamilton Anxiety Rating Scale total score before the treatment. Since great data scatter was observed for activities of GR and GST in both groups of patients, further determinations of both enzymatic activities in extended groups of patients would be prospective with the aims to select subgroups having abnormalities of glutathione metabolism, and to search for correlations of GR and GST activities with clinical psychopathological features.

A METHOD FOR RAPID EVALUATION OF TUMOR CELL PERCENTAGE IN BIOPSY SAMPLES

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Automated methods of determining local pathological changes in tissues are needed to develop new approaches for surgery and therapy, taking into account the accumulated knowledge on cell— and molecular-level characteristics of these changes.

Tumor cell percentage (TCP) in biopsy samples is a crucial value, determining if the particular sample is suitable for detailed and time-consuming diagnostic procedures, including permanent section histopathology and immunohistochemistry tests. Currently TCP is determined using frozen section histopathology, taking approximately half an hour and routinely performed during surgery. A method of rapid TCP evaluation would serve to improve throughput of histopathological laboratory, and possibly decrease surgery time.

Moreover, the TCP is in itself a characteristic of what the surgeon is cutting, so a rapid determination method (on the order of a few minutes), if developed, can be used to support decision making during surgery.

Currently, mass spectrometry-based methods of determination of tumor margins and infiltration areas are developed[1]–[3]. These methods can provide necessary information in about a minute, and can be deployed to determine TCP in tissue samples.

In this work, a protocol is proposed to estimate TCP in brain tissue samples undergoing mass spectrometry, based on several histological analyses of adjacent samples. Using this protocol and mass spectrometry data, it is possible to apply machine learning to determine TCP using only mass spectrometry in future samples. The protocol assumes macroscopically smooth TCP distribution and wide infiltration area, so it works best with highly malignant tumors.

The protocol was applied to samples from 20 patients with grade 4 glioblastoma, and 7 patients with non-tumorous pathologies. Using the data, XGBoost regressors were constructed and validated, with 80% of samples randomly chosen for training set and 20% for validation set. Resulting coefficient of determination was 97%.

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1. V. Pirro, C. M. Alfaro, A. K. Jarmusch, E. M. Hattab, A. A. Cohen-Gadol, and R. G. Cooks, “Intraoperative assessment of tumor margins during glioma resection by desorption electrospray ionization-mass spectrometry,” *Proc. Natl. Acad. Sci. U. S. A.*, vol. 114, no. 26, pp. 6700–6705, 2017.
2. J. Balog *et al.*, “Intraoperative tissue identification using rapid evaporative ionization mass spectrometry,” *Sci. Transl. Med.*, vol. 5, no. 194, 2013.
3. S. I. Pekov *et al.*, “Inline cartridge extraction for rapid brain tumor tissue identification by molecular profiling,” *Sci. Rep.*, vol. 9, no. 1, p. 18960, Dec. 2019.

DNA METHYLATION OF THE *ELOVL2*, *GRM2*, *F5*, *ZYG11A* AND *KLF14* GENES FOR AGE PREDICTION FROM BLOOD SAMPLES

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Blood is the most common biological samples at the crime scene. Criminalists are interested in the possibility of predicting the age of an unknown person from biological samples left at the crime scene. Chronological age can be determined using CpG markers analysis. The purpose of the study is to calculate the values of the correlation coefficients (R) and determination (R^2) for CpG markers in the *ELOVL2*, *GRM2*, *F5*, *ZYG11A* and *KLF14* genes to prove

the chronic age of an unknown individual based on analysis of blood samples, as well as assessing the accuracy of predicting chronological age based on a regression model.

Blood samples were collected from 88 people of Belarusian nationality (24 male and 64 female) aged 20 to 86 years using procedures approved by Bioethics Committee of The Institute of Genetics and Cytology of the National Academy of Sciences of Belarus, Minsk, Belarus. We analyzed 5 CpG-markers: cg16867657 (*ELOVL2*), Chr3:51741152 (*GRM2*), cg16054275 (*F5*), cg06784991 (*ZYG11A*), cg14361627 (*KLF14*). The age-relatedness of selected CpG candidates was investigated using methylation SNaPshot. We calculated in SPSS v.20.0 software Spearman correlation coefficients using the bootstrap function (1000 samples), 95% confidence interval, the determination coefficients R^2 (and corrected R^2), the median absolute deviation (MAD), the root mean square error (RMSE). Methylation level data were normalized using a non-linear transformation within [0, 1].

As a result, we obtained the following results (the table). The highest calculated R coefficients were obtained for markers cg16867657 (*ELOVL2* gene), cg14361627 (*KLF14* gene) and cg16054275 (*F5* gene).

	CpG markers				
	cg16867657 (*ELOVL2*)	Chr3:51741152 (*GRM2*)	cg16054275 (*F5*)	cg06784991 (*ZYG11A*)	cg14361627 (*KLF14*)
LL 95%	0,572	0,297	-0,704	0,223	0,422
R	**0,710**	**0,487**	**-0,560**	**0,440**	**0,613**
HL 95%	0,818	0,631	-0,396	0,626	0,766
p-level	9,98E-15	1,47E-06	1,45E-08	1,81E-05	2,13E-10

When all 5 CpG markers for the «Training dataset» (70% of the sample size) were included in the regression model, the age prediction error was within MAD = 4.25 years (RMSE = 0.55, R^2 = 0.744), for the «Testing dataset», similar values were MAD = 5.61 years (RMSE = 0.79, R^2 = 0.874). As part of the analysis on the impact on the change in the coefficient of determination (R^2), the CpG markers are arranged in the following sequence: cg16867657 (R^2 = 0.486), cg16054275 (+0.168 to the previous value of R^2), cg14361627 (0.078), cg06784991 (0.007), Chr3:51741152 (0.003).

The study was realized within the framework of the Union State Scientific and Technical Program “Development of innovative genogeographical and genomic technologies for identifying individuals and individual human characteristics based on studying gene pools of Union State regions” (“DNA Identification”), Activity No 2 “Development of a method for determining the probable age of an individual characteristic of its DNA” (Minsk, Republic of Belarus).

DNA METHYLATION-BASED AGE PREDICTION FROM BUCCAL SWAB SAMPLES: THE LEVEL OF METHYLATION OF 6 CPG MARKERS

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Background and Objectives. Buccal epithelium is one of the most common biological samples at the crime scene. Criminalists are interested in the possibility of predicting the age of an unknown person from biological samples left at the crime scene. Chronological age can be determined using CpG markers analysis. For buccal epithelium, such markers in the *KLF14*, *TSSK6*, *SST*, *TBR1*, *SLC12A5*, and *CNGA3* genes.

Purpose. The purpose of the study is to calculate the values of the correlation coefficients (R) and determination (R^2) for CpG markers in the *KLF14*, *TSSK6*, *SST*, *TBR1*, *SLC12A5*, and *CNGA3* genes to prove the chronic age of an unknown individual based on analysis of buccal epithelium samples, as well as assessing the accuracy of predicting chronological age based on a regression model.

Methods. In this study the methylation level of 6 CpG markers for buccal swab samples was analyzed for 82 people of Belarusian nationality using SNaPshot technology — cg14361627 (*KLF1*), cg08928145 (*TSSK6*),

cg00481951 (*SST*), cg12757011 (*TBR1*), cg07547549 (*SLC12A5*), cg19671120 (*CNGA3*). We calculated in SPSS v.20.0 software Spearman correlation coefficients using the bootstrap function (1000 samples), 95% confidence interval, the determination coefficients R^2 (and corrected R^2), the median absolute deviation (MAD), the root mean square error (RMSE). Methylation level data were normalized using a non-linear transformation within [0, 1].

Results. The highest calculated R coefficients were obtained for markers cg07547549 (*SLC12A5*), cg14361627 (*KLF14*) and cg12757011 (*TBR1*). When all 6 CpG markers for the «Testing dataset» MAD = 4.69 years (RMSE = 1.39, R^2 = 0.620). As part of the analysis on the impact on the change in the coefficient of determination (R^2), the CpG markers are arranged in the following sequence: cg14361627 (R^2 = 0.581), cg19671120 (+0.099 to the previous value of R^2), cg08928145 (0.053), cg00481951 (0.016), cg07547549 (0.005), cg12757011 (0.001)

Conclusion. Thus, using 6 CpG markers, we can predict chronologic age from samples of buccal epithelium with an accuracy of no worse than 5 years. In the future, we will expand the group of studied samples and reduce the prediction error.

Conflict of interests. The authors declare no conflict of interests.

CLINICO-LABORATORIAL AND URODYNAMIC DEVIATIONS AMONG CHILDREN WITH OVERACTIVE BLADDER

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Research objective. To identify clinico-laboratorial and urodynamic deviations among children with OAB.

Materials and methods. The study is based on examination of 20 somatically healthy children of 7-10 years old with the following complaints: sudden irresistible urges to urinate, that could be hardly restrained with or without imperative urge incontinence; frequent urination in small portions during the day; frequent awakenings during the night due to the emerging urge to urinate and involuntary urination at night. All children have been examined clinically (identification of the level of homocysteine, registration of the rhythm of urination (by keeping a diary of urination)) and through instrumental methods: uroflowmetry, ultrasound examination of the bladder with identification of the volume of residual urine, electroencephalography.

Results. After the examination, the following abnormalities were identified among the majority of the patients: hyperhomocysteinemia (direct evidence of impaired conduction and synergy of nerve impulses between neurons in the structures of the brain, since homocysteine was a marker of damage to enzymatic systems, indicating the metabolism of nerve cells; its increase reflected impairment of myelinesation of axonal structures of white matter and, consequently, impairment of the conduction of impulses between neurons of the brain); registration of the rhythm of urination showed that the predominant type was pollakiuria, which might be observed in frequent (more than 8 times a day) urination in small portions (among 60% of children), also enuresis (among 65%) and daytime urinary incontinence in the one third of the patients (30%) were diagnosed. On the basis of ultrasound examination of the bladder, it could be concluded that the one third of the children (33%) had an increase in the volume of residual urine (due to a decrease in the contractile function of the detrusor). By the uroflow method of research it was found out that among almost the half of the children (45%), the intermittent type of urination prevailed (in which the maximum and average urine flow rate was reduced, the time to reach the maximum speed was shortened), also rapid (30%) and non-obstructive (25%) types were diagnosed. According to the electroencephalography data, disorganization of the alpha rhythm, with a tendency to an increase in the number of beta rhythm waves was found.

Conclusion. Our research identifies the following clinico-laboratorial and urodynamic symptoms: hyperhomocysteinemia (in 30% of cases), pollakiuria (60%), enuresis (65%), daytime urinary incontinence (30%), prevalence of intermittent type of urination (45%), an increase in the volume of residual urine in the bladder (33%) and disorganization of the alpha rhythm with a tendency to an increase in beta rhythm waves according to electroencephalography.

PATIENT-SPECIFIC BIOMECHANICAL ANALYSIS IN COMPUTER-AIDED PLANNING OF DENTITION RESTORATION BASED ON DENTAL IMPLANTS

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Purpose. Individualization of medical treat is a hot points of today's medicine including implant dentistry. A computer simulation of the edentulous mandible restoration planning with implants placement under the scheme "All-on-4" was performed, based on evaluation of the stress-strain state of the components of the system under various loading conditions.

Methods. Mandible CT was done with the dental tomograph Galileos (Sirona). Image processing, including segmentation, creation of a three-dimensional triangulated surface model and a tetrahedral grid, was carried out in the MIMICS program complex. The model obtained was supplemented with implants models and passed on to the finite-element complex ANSYS, where numerical simulation was carried out. Titanium implants 10-11 mm long and 3.5 mm in diameter were taken. Different loading schemes were considered, corresponding to central (biting) and one-sided (chewing) occlusion. Central occlusion was modeled by applying vertical load to two central implants.

Results. Areas of stress concentration in the bone in all cases arose at the thread tops and carvings, and especially in the vicinity of the implant neck. Loading in the lateral part of the artificial dentition appeared more dangerous than in the frontal compartment.

Conclusions. The technology presented makes it possible to take into account individual geometric and mechanical characteristics of the bone structures and tissues of a particular patient in the digital planning of implantation on the edentulous jaw.

The work was done jointly with D.A.Gribov on the topic of state assignment (state registration number AAAA-A17-117021310386-3) and with partial support of RFBR grants №17-08-01579 and №17-08-01312.

PECULIARITIES OF THE METABOLIC STATUS, PATIENTS IN THE SHEET OF EXPECTATION FOR HEART TRANSPLANTATION

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The aim of the study was to evaluate the parameters of metabolic status in patients before orthotopic heart transplantation (OHT).

Materials and methods. In the cardiovascular pathology department of the Federal State Budgetary Institution of Nutrition and Biotechnology Clinic, 50 patients with severe heart failure, who are on the OHT waiting list, were evaluated for energy metabolism by indirect respiratory calorimetry with determination of daily nitrogen excretion and assessment of actual nutrition by frequency analysis.

The results showed that in patients before OHT, the energy value of the home diet is significantly higher (by 21.0% ($p < 0.05$) than the average in the population. Analysis of the balance of fat intake and oxidation showed that, despite the relative an increase in fat intake with food compared to normal (by 41.2%), patients have an even greater increase in the rate of fat oxidation, as a result, the balance of fat intake and oxidation in these patients acquires negative values (-68.2%). sharing revealed even rougher imbalance: carbohydrate intake is 31.3% higher than the reference values, and the carbohydrate oxidation rate is 25.0% lower.The analysis of protein intake and oxidation did not reveal significant violations, which reflects the balanced nutrition of patients according to this indicator and does not require dietetic correction.

Conclusion. TThe data obtained confirm the hypothesis of the presence of a pronounced metabolic shift in patients before OHT.

The study was conducted in the framework of the scientific theme №0529-2019-0061. The source of funding is the federal budget.

PECULIARITIES OF THE METABOLIC STATUS OF PATIENTS WITH OBESITY AND OBSTRUCTIVE SLEEP APNEA SYNDROME

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Objective: to study the metabolic status in obese patients complicated by the development of obstructive sleep apnea syndrome (OSAS).

Materials and methods: 422 obese (O.) patients were examined. Depending on the severity of obesity, all patients were divided into three groups. A comprehensive assessment of metabolic status was carried out: including analysis of actual nutrition, assessment of bioimpedansometry, assessment of energy metabolism parameters. Cardiorespiratory monitoring of night sleep was performed to diagnose obstructive sleep apnea syndrome.

Results. In patients with obesity and OSAS, excess calorie intake, fat and carbohydrate intake were revealed. An increase in the content of fat mass and total body fluid. In patients with obesity II degrees and OSAS revealed significantly ($p = 0.018$) higher basic metabolism (BM) than in the group of patients with O. II degrees and without OSAS. Similarly in the group with O. III degrees and OSAS, the BM indicators were also significantly higher than the corresponding indicators in the group with O. III degrees without OSAS ($p = 0.01$). In patients with O. III degrees and OSAS also revealed a significant ($p <0.05$) increase in the rate of fat oxidation compared to O. II degrees, and a significant ($p <0.05$) decrease in the rate of oxidation of carbohydrates.

Conclusion. Obesity in combination with OSAS is accompanied by pronounced changes in the metabolic status of patients, which justifies the need for optimization and individualization of diets in this category of patients.

CUTTING-EDGE MULTI-LEVEL ANALYTICAL AND STRUCTURAL CHARACTERIZATION OF ANTIBODY-DRUG CONJUGATES: PRESENT AND FUTURE

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The development and optimization of antibody drug conjugates (ADCs) rely on improving their analytical and bioanalytical characterization, by assessing critical quality attributes (CQAs). Among the CQAs, drug load distribution (DLD), the amount of unconjugated antibody (D0), the average drug-to-antibody ratio (DAR), the drug conjugation sites and the residual drug-linker and the glycan-profile, in addition to high and low molecular weight species (H/LMWS), and charge variants are the most important ones. The characterization of such complex molecules requires for a complementary analytical toolbox.

The presentation discusses the analytical and structural toolbox for the characterization of first, second and third generation of ADCs focusing on state-of-the-art liquid chromatographic (LC) techniques including size exclusion (SEC), hydrophobic interaction (HIC), reversed phase (RP) and hydrophilic interaction (HILIC) liquid chromatography. In addition to unidimensional separations, the potential of multi-dimensional liquid chromatographic techniques will also be demonstrated. By applying RP in the second dimension of a comprehensive two-dimensional (LC x LC) setup, the inherently not mass spectrometry compatible non-denaturing LC modes (e.g. HIC) can be coupled indirectly to mass spectrometric detection (HIC x RP — MS) which offers lots of benefits. These emerging techniques allow a deep insight into important CQAs that are related to ADC Chemistry Manufacturing and Control (CMC) as well as an improved understanding of in vitro and in vivo ADC biotransformations. Some future perspectives and trends will also be mentioned.

NUCLEIC MAGNETIC RESONANCE AND PROTEOME ANALYSIS FOR THE ASSESSMENT OF ARTICULAR HYALINE CARTILAGE TYPE II COLLAGEN IN EARLY SIGNS OF KNEE OSTEOARTHROSIS

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The examination of 36 patients of both sexes aged 38-50 years with 0-I stages of primary osteoarthrosis (OA) included the assessment of urinary type II collagen fragments 24-h extraction (Urine CartiLaps® (CTX-II) EIA assay), T2 Relax mapping, T2-relaxometry of the articular cartilages in 1.5T Hitachi Echelon CT scanner. CT scans were taken in axial and sagittal planes and processed with the software graph editor. We chose ROIs in the articular cartilage plane of medial femoral condyles corresponding to areas with various biomechanical loading to run quantification of T2-relaxometry time.

The statistical analysis of the results with the Mann-Whitney U-test revealed a significant augmentation ($p<0.05$) of urinary type II collagen fragments 24-h extraction — 4.21 (3.05; 8.19) μg/day compared to the control values — 2.20 (1.08; 3.44) μg/day. Under Spearman's coefficient ($R=0.6$) the amount of type II collagen extraction per day correlated ($p<0.05$) to the difference of T2-relaxometry value found between ROIs of the loaded and intact areas of articular cartilage constituting 10 to 17 percent on average.

Conclusion: The specifics of metabolism and structural distribution of type II collagen in articular cartilage in early signs of primary OA are associated with the augmentation of 24-h urinary extraction of its degradation products as well as the increase of its anisotropy on T2-relaxometry evidence.

HOMOCYSTEINE IN THE PATHOGENESIS OF INFERTILITY

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Infertility is the cause of at least half the cases of infertility in marriage and is a serious medical and social problem. A complex of exogenous influences associated with changes in lifestyle and environmental conditions is considered as the main mechanism for impaired fertilization ability.

Objective: To assess the relationship of homocysteine levels in seminal plasma and sperm with morphofunctional parameters of the ejaculate in the genesis of infertility.

Methods and results: The study involved 60 infertile men — patients of assisted reproductive technology clinics aged 20-43 years. The comparison group consisted of 46 fertile men. Homocysteine concentration was determined using a commercial Homocyctein EIA enzyme immunoassay (Great Britain). Homocysteine is called as one of the candidates for the role of predictor of reproductive pathology. The importance of this amino acid in the development of pathospermia remains a matter of discussion. We have revealed an uneven distribution of homocysteine with accumulation in spermatozoa and an insignificant and unreliable decrease in its concentration in the ejaculate. Based on this, it can be assumed that the definition of a substance in isolation only in the ejaculate or sperm plasma does not give a true picture of its metabolism, followed by a false interpretation of the results. Close correlations were also found between pathospermia and homocysteine content both in whole ejaculate and in spermatozoa.

Conclusions. The findings suggest that sperm accumulation of homocysteine as a product of methionine transmethylation may represent the molecular basis for suppressing the activity of folate-dependent enzymes involved in the reproduction function.

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METABOLOMIC SIGNATURES OF HEAD AND NECK CANCER IN BIOFLUIDS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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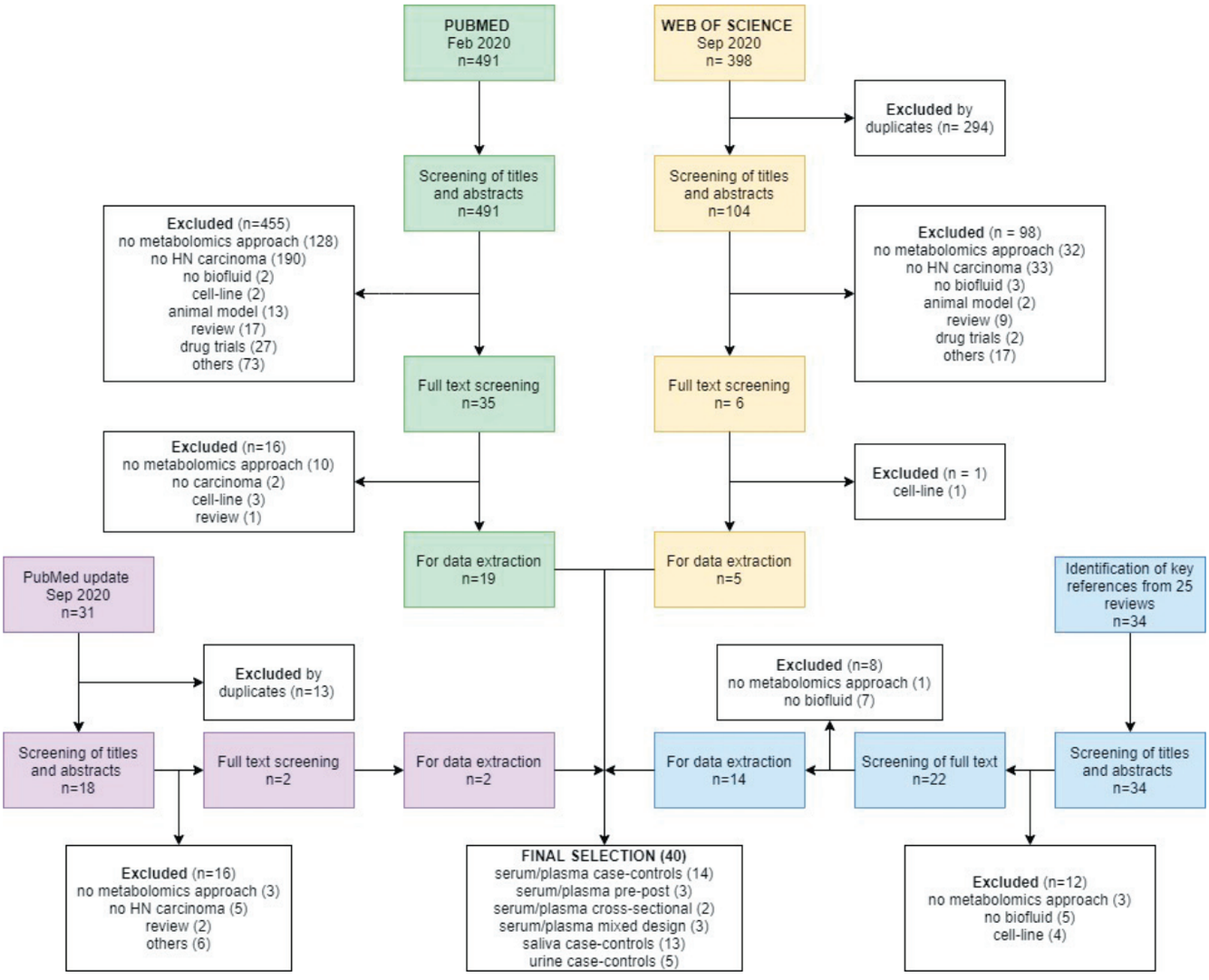
Background: Head and neck cancer (HNC) is the 6th most common malignancy worldwide. Metabolomic analysis has arised as a new non-invasive method for early diagnosis.

Objective: To systematically review available evidence from metabolomic analysis performed in HNC.

Methods: Systematic search executed in 2020 using PubMed and Web of Science. Metabolomic studies performed in biofluids were examined.



Results: 889 publications were initially identified. The final number of eligible studies for data extraction was 40[(serum/plasma: 14 case-control, 3 pre-post treatment, 2 cross-sectional and 3 mixed design), (saliva: 13 case-control), urine: 5 case-control)] after screening of titles, abstracts and full texts. Relevant reviews and list of references were examined. Most of the studies reported amino acids (i.e. leucine and serine) and sugars (i.e. glucose and galactose) to be significantly altered in HNC. Examples of metabolic pathways impacted in HNC include methionine and galactose metabolism, threonine and alanine metabolism, among others. Data quality assessment and meta-analysis are in ongoing phase.

Conclusions: Metabolomics has been extensively used in HNC research. Most of the studies have been conducted in serum/plasma comparing disease versus control groups. Specific metabolites that can potentially serve as non-invasive biomarkers will be proposed through meta-analysis.

OBESITY AND ARTERIAL STIFFNESS IN WOMEN OF DIFFERENT AGES

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Introduction: obesity, especially its abdominal type, is a significant risk factor for cardiovascular disease (CVD) for women and is associated with the development of atherosclerotic changes in the vascular wall.

Purpose: to study the relationship of obesity with indicators of arterial stiffness and daily dynamics of central aortic pressure in women of different age groups.

Materials and methods: 161 women were examined, which were divided into 3 groups: 1st group — 52 young women from 18 to 30 years old (23.8±5.3 years old); 2nd group — 54 women from 31 years old until menopause (41±5.9 years); group 3 — 55 women in the postmenopausal period (55.4±5.8 years). All volunteers underwent questionnaires, anthropometry, the study of arterial stiffness with the Doppler method and the method of volume sphygmography, daily monitoring of blood pressure with an assessment of vascular stiffness and central aortic pressure.

Results: in 1st group abdominal obesity correlates with an increase in the aortic pulse wave velocity PWVao (R=0.41, p=0.002) and pathological changes in the characteristics of the reflected wave. In 2nd group general obesity is more associated with an increase in central and peripheral pressure: SBP (R=0.43, p=0.001), SBPao (R=0.38, p=0.01), PP (R=0.44, p=0.001), PPao (R=0.45, p=0.001). Abdominal obesity in the 2nd group correlates with an increase in the carotid-femoral pulse wave velocity cfPWV (R=0.4, p=0.003) and is less correlated with pressure. In the 3rd group identified correlations of abdominal obesity with PWVao (R=0.33, p=0.01), cfPWV (R=0.32, p=0.02), PPao (R=0.3, p=0.02), PP (R=0.33, p=0.01).

Conclusion: general and abdominal obesity are interrelated with arterial stiffness and an increase in central and peripheral pressure in women of various ages. This factor is most significant for women with preserved reproductive function. Evaluation of arterial stiffness in obese women will allow the timely formation of risk groups and preventive and therapeutic measures.

PDX1 INCREASES ADHESION AND DECREASES MOTILITY OF PANCREATIC CANCER CELLS

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Cell-to-cell interactions and cell adhesion are key mediators of cancer progression. In particular, these interactions are responsible for immune evading, cell migration and metastasis. Restoring adhesion between tumor and surrounding cells or extracellular matrix can be considered as approach to controlling cancer migration.

Previously we showed that ectopic expression of PDX1 gene leads to reduce the motility of pancreatic cancer cells. Now we hypothesized that the suppression of migration properties may be associated with the effect of PDX1 on cell adhesion. Analysis of proliferation showed that PDX1 gene increases the rate of cell growth. The analysis of directed and undirected cell migration demonstrated low motility level of Colo357 and PANC-1 cells expressing PDX1. Analysis of the gene expression revealed that ectopic expression of the PDX1 gene in Colo357 and PANC-1 cells leads to decreasing expression levels of migration associated genes and increasing of expression level of genes negatively affecting cell motility. Comparison of the adhesive properties revealed that ectopic PDX1 expression increases the level of cell adhesion PANC-1 and Colo357 cells to type I collagen, fibronectin, and poly-L-lysine.

Thus, it can be assumed that ectopic expression of PDX1 decreases the migration potential of cancer cells by increasing the adhesive properties of cells.

The study was supported by the Russian Science Foundation (project no. 19-15-00317).

ASSESSMENT OF THE TOXIC MECHANISM ROLE IN MYOCARDIAL DAMAGE IN PATIENTS WITH CANCER CACHEXIA BASED ON STRUCTURAL CHANGES

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Despite progress in the treatment of patients with cancer, in most cases it's not possible to achieve a significant increase of life-expectancy. These patients already have cancer cachexia (CC), which's associated with an unfavorable prognosis and a myocardium damage. The cause of death mostly is left-sided heart failure (LSHF). One of the lesion leading mechanisms is toxic one. The objective of this work: study of structural changes in myocardium of patients with CC who died of LSHF for determining the role of toxic myocardial damage.

For the material has served 20 cases, 15 of which were palliative patients with CC, 5—control cases (death of intoxication due to pancreonecrosis). We've analyzed clinical and structural data on autopsy materials of myocardium and lungs using polarizing microscopy.

All patients with CC had an increase in hydrostatic and/or decrease in oncotic pressure and histologically confirmed pulmonary edema, which indicates LSHF. Regular light microscopy revealed myocardial atrophy and areas of dystrophic changes. The myocardium of the control cases wasn't atrophic, with loss of striations. Using polarizing microscopy, it's possible to identify a toxic-damage marker—contractures of myocardium. While researching myocardium of control cases, contractures were found; of CC-patients—weren't detected.

The absence of toxic damage markers can be explained by the fact that the metabolic processes in myocardium in CC are so slowed down that the impact of tumor decay products doesn't significantly affect the myocardium and doesn't play an important role in the formation of lesion. This indicates a different mechanism of damage.

DETECTION OF MUTATIONS ASSOCIATED WITH THE DEVELOPMENT OF CANCER BY PYROSEQUENCING

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Determination of germinal and somatic mutations associated with the development of cancer is widely used for the diagnosis of hereditary oncologic syndromes, determining the predisposition to the development of malignant neoplasms, confirmation of the diagnosis, treatment management and monitoring, predicting treatment response and the risk of relapse. A pyrosequencing-based approach allows detecting different types of mutations, and, if necessary, quantifying the mutant and intact allele ratio.

For the detection of frequent germinal mutations in the *BRCA1*/2 genes, the "BRCA-screen" test (part of the "AmpliSens® Pyroscreen" kit) was developed. The "BRCA-screen" test allows identifying following mutations: 5382insC (rs80357906), 4153delA (rs80357711), 300T>G (C61G, rs28897672), 2080delA (rs80357522) and 185delAG (rs80357914) in *BRCA1* gene, and 6174delT (rs80359550) in *BRCA2* gene. Additionally the pyrosequencing technique for frequent mutations allows to detect the rare substitutions in sequenced fragments (for example, rs80357783 (BRCA1 185insA) and rs80357407).

The driver mutations in *BRAF*, *KRAS*, *HRAS* and *NRAS* genes are associated with different cancers and response to targeted kinase inhibitors treatment. The high frequency of mutations in the *BRAF* gene allows using the appropriate tests for diagnosis of malignancy. The method for sequencing 592-601 *BRAF* codons has been developed, method allows to identify all hot spots in this region, including the most frequent mutation p.V600E (c. 1799 T>A). The identification of mutations in 592-601 codons is realized by discrimination algorithm based on pyrogram signals values. This approach allows determining 2% of the mutant allele for V600R and V600K, and 3% for V600M and V600E. The method for detection mutations in the *KRAS* gene (PMID: 24340949) allows us to quantify all possible mutations in 12-13 codons with 3% limit of detection. Currently, the similar mutations detections methods for 12, 13, and 61 codons of the HRAS and NRAS genes are being developed.

The detection of somatic mutations in the *JAK2, MPL*, and *CALR* genes is used in the differential diagnosis of chronic myeloproliferative neoplasms, for monitoring the level of clonal hematopoiesis and evaluating the effec-

tiveness of therapy. The detection of V617F mutation in *JAK2* gene is possible by combination of PCR and pyrosequencing methods. The "TROMBO-screen" test (part of the "AmpliSens® Pyroscreen" kit) allows to perform quantitative assay (PMID: 25850251), allele-specific PCR can increase the sensitivity up to 0.25% mutant fraction (PMID: 30615403). Other developed pyrosequencing-based methods allow detecting the driver mutations in exon 12 of *JAK2*, and identifying the most common mutations in exon 9 of the *CALR* gene and in exon 10 of the *MPL* gene.

Currently, in the Central research institute of Epidemiology sets of reagents and kits for determining germinal and somatic mutations that can be used in clinical and scientific practice to solve a wide range of problems is developing or has already manufactured.

PROPERTIES OF BIOGENIC CHLORAMINE OXIDANTS CONTAINING AN ADENINE RESIDUE AND MODIFYING SULFUR-CONTAINING PROTEIN TARGETS

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Objective: To synthesize stable chloramine derivatives of structural analogs of adenine and to establish their physico-chemical properties. It is planned to create covalent inhibitors of receptors of adenosine agonists in order to regulate platelet functions.

Methods: Quantum mechanical calculations of molecular characteristics that determine the reactivity of chloramines under study were performed *ab initio* using the GAMESS program. An experimental study of the interaction of structural analogs of N-chloroadenine with sulfur-containing groups of proteins, peptides, amino acids was carried out by the kinetic spectrophotometry.

Results: By analyzing the correlation between calculated charges of active chlorine and the reaction rate constants for known chloramine derivatives of amino acids and related compounds, the potential reactivity of various structural analogs of N-chloroadenine with respect to a sulfhydryl group was estimated. It was found that such chloramines react with sulfur-containing compounds with a stoichiometric coefficient close to 1.0. The reaction rate constants for studied chloramines with methionine and fibrinogen were estimated; they were about 1.5 and 90 $M^{-1}s^{-1}$, respectively. The rate constants of reactions of structural analogs of N-chloroadenine with glutathione, cysteine and acetylcysteine exceeded 10^5 $M^{-1}s^{-1}$; the rate constant for the reaction with serum albumin was of the same order.

Conclusion: A number of chloramine derivatives of structural adenine analogs have been synthesized. It has been shown that their ability to chemically modify sulfur-containing compounds, including proteins, is characterized by their selectivity towards thiols.

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THERAPEUTIC DRUGS FOUND IN HAIR AND URINE OF SUBJECTS UNDERGOING DETOXIFICATION TREATMENTS

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Human hair retains traces of the drugs taken during hair growth keeping a record of drug use history over a rather long period. Each centimetre of hair keeps record of the drug intake corresponding approximately to one month. Consequently, hair has been used for decades as an alternative matrix in the control of chronic abuses of narcotics. Much less attention has been paid to the possible use of this matrix to monitor the compliance to pharmaceutical treatment of chronic illnesses, such as diabetes, hypertension, hypercholesterolemia, epilepsy, psychiatric disorder, etc.

The main analytical problem in hair analysis is related to the small amounts of samples which can be collected and the small concentrations of analytes present in the matrix. For this reason only high sensitivity techniques (typically chromatographic techniques with mass spectrometers, GC-MS and LC-MS) can be applied. Indeed in addition to high quality instrumentation also highly qualified and specialized personnel is needed. This limits the possibility of performing hair analysis to the best equipped laboratories of analytical chemistry and toxicology.

In this context, a novel LC-MS instrument, tailored to be used with a "push-button" approach, has recently been introduced in the market (ToxTyper™, Bruker Daltonics) offering an interesting possibility of enlarging the application of hair analysis. This analytical platform is based on a UHPLC unit coupled to an ion trap mass spectrometer (MS) and offers rapid, qualitative broad spectrum screening of drugs and metabolites using a proprietary library including over 5000 compounds.

To test its suitability for monitoring the compliance to therapy, in the present work, the method has been tested for the determination of therapeutic drugs and their metabolites in the hair of subjects undergoing controls for the monitoring of abstinence from narcotic drugs.

The reported analytical method is based on a simple hair pre-treatment consisting of an overnight acid incubation in 0.1 mol/L HCl, followed by direct injection. The separation was then performed using a reverse-phase column with a rapid gradient elution of 11 minutes (from 1% acetonitrile in 0.1% ammonium formate to 95% acetonitrile in 0.1% ammonium formate). Detection was by a fast ion trap analyzer (32,500 m/z sec−1) operating in the mass range 70-800 m/z. The chromatographic retention time and MS2/MS3 data were used for compound identification using a proprietary database which allowed to screen for up to 987 compounds.

In the present preliminary study, the proposed approach proved suitable for the rapid broad spectrum screening of hair samples, including not only drugs of abuse but, interestingly, several classes of therapeutic drugs for which adherence to therapy is highly recommended.

PERSONALIZED THERAPY FOR DEPRESSION IN ELDERLY PATIENTS

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Conduction. Increasing the effectiveness of therapy for late-age depression is possible when adding neuroprotective and neurotrophic drugs to antidepressants. It is necessary to develop reasonable indications for their appointment based on the selection of predictors of low therapeutic response (NTO)

Material and methods. Hospitalized patients 60 years and older with mild to moderate depression (ICD-10) received mono-depressive therapy (44 people) and complex therapy with the same antidepressants in combination with neuroprotective drugs (108 people). Predictors of NTO were identified in the group with monotherapy using nonparametric correlation analysis between changes in the average total scores of the HAMD-17 scale and socio-demographic, clinical, somatic and neuroimaging (brain CT) parameters. The effectiveness of treatment of patients with predictors of NTO against the background of mono-and complex therapy was compared.

Results. Predictors of NTO ($p<0.05$) in elderly depressive patients were solitary living (-0.426), the presence of complaints of memory loss (-0.397) and signs of pronounced diffuse damage to the subcortical white matter of the brain (-0.319). Patients with NTO predictors are significantly more likely ($p<0.05$) to be nonresponders, and the effectiveness of therapy significantly decreases ($p< 0.001$) when the number of predictors increases to 2 or more.

Conclusion. Personalized indications for the augmentation of neuroprotective drugs for antidepressant therapy at a later age are the presence of 2 or more predictors of NTO in patients.

MMSE AND MOCA IN LATE-ONSET PSYCHOSIS: DYNAMIC DURING INPATIENT TREATMENT AND CORRELATION WITH OTHER COGNITIVE TESTS

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Background. It is important to detect cognitive dysfunction in patients with late-onset schizophrenia for it correlates with functional disability. We aimed to assess validity of screening instruments through repeated measurements and accordance to other cognitive tests.

Methods. 42 patient with late-inset schizophrenia (age 64,1±9,2, 88% females) and 12 patients with late-onset schizoaffective disorder (age 63,9±5,3, 50% females) underwert psychiatric and cognitive examination: MMSE and MoCA by admission and/or after 4-6 weeks; FAB, verbal and visual memory, trail making test (TMT, part A, B) at the 2nd time point, PANNS and HDRS-17 at both time points. MoCA was applied in both time-points in 36 patients, MMSE — in 43 patients. Wilcoxon test and Spearman correlations were used.

Results. MMSE and MoCA scores increased significantly after 4-6 weeks of treatment: MMSE from 25,0 to 26,4 (p=0,004); MoCA from 20 to 21,6 (p=0,009); attention, memory, orientation subscales of MoCA changed significantly. MMSE at the 2nd time point correlated with initial MMSE (r=0,724, p<0,001) and MoCA at the 2nd time point (r=0,686, p<0,001), initial MoCA correlated with MoCA at the 2nd time point (r=0,600 p<0,001). By admission MMSE and MoCA scores correlated with negative (r=-0,324, p=0,036 and r=-0,463, p=0,005, respectively) and general (r=-0,324, p=0,030 and r=0,425, p=0,011, respectively) symptoms scores; MMSE — with HDRS-17 (r=-0,329, p=0,036). At the 2nd time point both MMSE and MoCA correlated with severity of negative (r=-0,569, p <0,001 and r=-0,580 p <0,001, respectively) and general symptoms (r=-0,487, p <0,001 and r=-0,455, p=0,001, respectively). At the 2nd time point MMSE and MoCA correlated with FAB (r=0,323, p=0,027 and r=0,501, p<0,001, respectively), immediate (r=0,524, p<0,001 and r=0,479, p=0,001, respectively) and delayed (r=0,488, p=0,001 and r=0,455, p=0,003, respectively) verbal memory recall, immediate (r=0,362 p=0,017 and r=0,524, p<0,001, respectively) and delayed (r=0,362, p=0,017 and r=0,579, p<0,001, respectively) visual memory recall, performance time of TMT part B (r=-0,422, p=0,007 and r=-0,709, p<0,001). MoCA but not MMSE correlated with performance time of TMT part A (r=-0,571, p<0,001) and number of errors in TMT part B (r=-0,412, p=0,010). No correlations with medication dose was found.

Conclusion. MoCA and MMSE are reliable screening instruments. They are recommended to apply in remission phase for their scores correlate with depressive and general psychotic symptoms severity. MoCA is more preferable due to stronger correlations with executive dysfunction tests.

LEUKOARAIOSIS ON CT IN PATIENTS WITH LATE-ONSET SCHIZOPHRENIA (LOS) AND SCHIZOAFFECTIVE DISORDER (LOSAP) CORRELATES WITH NUMBER OF PSYCHOTIC EPISODES, COGNITIVE DYSFUNCTION AND LENGTH OF HOSPITAL STAY

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Background. Late-onset psychosis is frequently associated with subsequent development of major neurocognitive disorder. Appearance of leukoaraiosis on MRI scans increases risk of dementia and depression, whereas leukoaraosis on CT is a sign of more severe brain pathology which is strongly associated with neurological signs (Marek et al., 2018). This study aimed to assess frequency and clinical correlates of leukoaraiosis on CT in patients with late-onset psychosis.

Method. Patient with DSM-V diagnosis of late-onset schizophrenia (n= 43, age 65,2±9,4; 90% females) and late-onset schizoaffective disorders (n=9, age 64,9±5,8; 30% females) underwent CT by admission and cognitive examination (MMSE, MoCA. FAB, verbal and symbolic memory, trail making test (part A, B) in recovery before discharge. Severity of psychiatric symptoms was assessed by PANNS and HDRS17 at both time points. Spearman correlations of leukoaraiosis and clinical parameters were calculated.

Results. The frequency of leukoaraiosis was 28.6% in LOS patient and 44,4% in LOSAP group. Leukoaraiosis on CT correlated with age (*r= 0,398, p=0,008*), number of episodes (*r=0,503, p=0,001*), lower MMSE score (*r=-0,342, p=0,055*) and lower immediate verbal memory recall (*r=-0,335, p=0,070*), increased time in TMT part B (*r=0,353, p=0,071*), prolonged hospital stay (0,345, p=0,024). No correlation between leukoaraiosis and positive, negative and general symptoms PANNS score as well as HDRS score was found.

Conclusion. One third of patient with late-onset psychosis has leukoaraosis on CT which correlates with cognitive dysfunction and prolonged hospital stay. Correlation between leukoaraiosis and number of psychotic episodes may reflect progression of brain pathology due to psychosis.

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SULFORAPHANE — INHIBITOR FOR 2019-NCOV CORONAVIRUS M PROTEASE: A DFT INVESTIGATION

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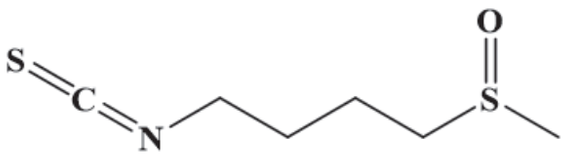

Sulforaphane

In the present work, first time the molecular structure of the Sulforaphane has been investigated using Density Functional Theory (DFT/B3LYP/6-311+G*) in solvent water. The molecular HOMO-LUMO, UV/Vis, excitation energies and oscillator strengths of investigated compound have also been calculated and presented. NBO analysis has been calculated in order to elucidate the intramolecular, rehybridization and delocalization of electron density. In order to find candidate drugs for 2019-nCoV Coronavirus M protease, we have carried out a computational study to screen for effective available the Sulforaphane which may work as a strong inhibitor for the M^{pro} of 2019-nCoV. The interaction of the Sulforaphane with the Coronavirus M protease 2019-nCoV were performed by molecular docking studies. It was found that the ligand Sulforaphane shows the best affinity towards of the M^{pro} 2019-nCoV compared to other known antiviral drugs: Colistin, Valrubicin, Icatibant, Bepotastine, Epirubicin, Epoprostenol, Vapreotide, Aprepitant in which the binding energy for Coronavirus M^{pro} 2019-nCoV and them is -11.206, -10.934, -9.607, -10.273, -9.091, 10.582, -9.892 and -11.376 kcal/mol that shows weak binding affinity between them and 2019-nCoV Coronavirus M^{pro}. The binding energy for Coronavirus M^{pro} 2019-nCoV and the ligand Sulforaphane is -37.156 kcal/mol in which shows good binding affinity between the ligand Sulforaphane and 2019-nCoV Coronavirus M^{pro}. The ligand Sulforaphane works as a strong inhibitor for the M^{pro} of 2019-nCoV.

VITAMIN B7 — INHIBITOR FOR 2019-NCOV CORONAVIRUS M PROTEASE: A DFT INVESTIGATION

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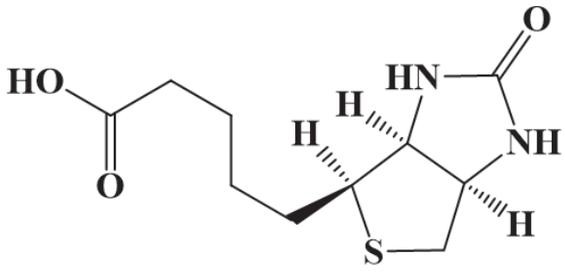
In the present work, first time the molecular structure of the Sulforaphane has been investigated using Density Functional Theory (DFT/B3LYP/MidiX) in solvent water. The molecular HOMO-LUMO, excitation energies and oscillator strengths of investigated compound have also been calculated and presented. NBO analysis has been calculated in order to elucidate the intramolecular, rehybridization and delocalization of electron density. In order to find candidate drugs for 2019-nCoV Coronavirus M protease, we have carried out a computational study to screen for effective available the Sulforaphane which may work as a strong inhibitor for the M^{pro} of 2019-nCoV. The interaction



Vitamin B_7

of the Sulforaphane with the Coronavirus M protease 2019-nCoV were performed by molecular docking studies. It was found that the ligand Sulforaphane shows the best affinity towards of the M^{pro} 2019-nCoV compared to other known antiviral drugs: Colistin, Valrubicin, Icatibant, Bepotastine, Epirubicin, Epoprostenol, Vapreotide, Aprepitant in which the binding energy for Coronavirus M^{pro} 2019-nCoV and them is -11.206, -10.934, -9.607, -10.273, -9.091, 10.582, -9.892 and -11.376 kcal/mol that shows weak binding affinity between them and 2019-nCoV. The binding energy for Coronavirus M^{pro} 2019-nCoV and the ligand Sulforaphane is -44.709 kcal/mol in which shows good binding affinity between the ligand Sulforaphane and 2019-nCoV. The ligand Sulforaphane works as a strong inhibitor for the M^{pro} of 2019-nCoV.

INVESTIGATION OF ENCAPSULATION OF TALZENNA DRUG INTO CARBON AND BORON-NITRIDE NANOTUBES [CNT(8,8-7) AND BNNT(8,8,-7)]

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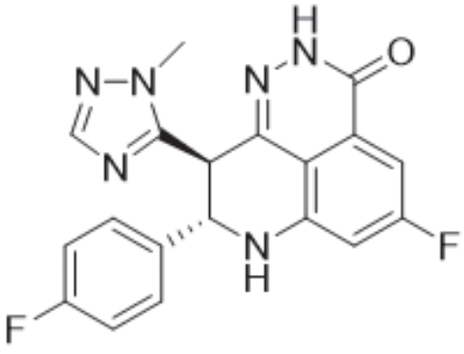

Chemical structure of Talzenna

The aim of this work is a study of the encapsulation and intermolecular non-bonded interaction of an anticancer drug Talzenna into carbon nanotube [CNT(8,8-7)] and boron nitride nanotube [BNNT(8,8-7)]. The interaction effect of Talzenna with the CNT and BNNT on electronic and adsorption properties were theoretically investigated in the solvent phase at the M062X/6-311G* level of theory for the first time. With the capsulation of Talzenna drug, the electronic properties of the CNT and BNNT nanotubes change. The electronic spectra of the Talzenna drug, complexes CNT/Talzenna and BNNT/Talzenna in the solvent water were calculated by Time Dependent Density Functional Theory (TD-DFT) for the study of adsorption effect. According to the natural bond orbital (NBO) results, all three molecules Talzenna, CNT and BNNT play as electrons donor and acceptors at the complexes CNT/Talzenna and BNNT/Talzenna. On the other hand, the charge transfer is occurred between the bonding, antibonding or nonbonding orbitals in molecules Talzenna, CNT and BNNT. Based on the results, CNT(8,8-7) and BNNT(8,8-7) can be used as a drug delivery system for the transportation of Talzenna as anticancer drug within the biological systems.

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MASS SPECTROMETRY MOLECULAR PROFILING AS AN ALTERNATIVE TO INTRAOPERATIVE HISTOLOGICAL EXAMINATION

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Extent of resection is a crucial factor affecting survival in patients with glial tumors and different MS based methods applied to solve this problem. Lipid profiling of malignant and intact tissues can be used for intraoperative navigation as well as rapid postoperative diagnosis clarification. It is possible to analyze overall spectra to find distinctive, differentiating features without the necessity of identification of each compound in spectra In this case, the alterations of relative intensities of multiple peaks became a “marker” that allows tissue differentiation In our study tissues samples (primary brain tumors and non-tumorous pathological brain tissues) were analyzed immediately using Inline Cartridge Extraction system combined with LTQ XL instrument. Other parts of samples were analyzed in the same way after a freeze thaw cycle using LTQ XL Orbitrap instrument to obtain high resolution. Pathology report was obtained for each sample. Afterwards all data were assigned to a particular pathology class and sets of distinctive features were highlighted using non tumor pathological tissues as a control. Accuracy and specificity for the classifiers based on the high-resolution data were 0,98 and 0,93 respectively (low-resolution data), accuracy and specificity for rapid profiling in the clinic and frozen samples analysis in the laboratory were 0,96 and 0,91 respectively. Amount of data collected with ambient mass spectrometry significantly enhancing the reliability of mass spectrometric approach for intraoperative tumor tissue differentiation and provide the new insights on the molecular mechanisms allowing such differentiation.

The research was funded from the RSF (project No. 16-15-10431).

THE ROLE OF POLYMORPHIC LOCI OF A VARIETY OF GENES IN THE DEVELOPMENT OF GAMBLING IN THE REPUBLIC OF BELARUS

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Pathological gambling is an uncontrollable urge to carry out gambling practice despite the negative impact on the life and health of the individual. Game process is able to stimulate the brain’s reward system in the same way that drugs or alcohol can, leading to addiction. It is known that gambling addiction is a multifactorial disorder, but the genetic factor is the most interesting in the genesis of this pathology.

This study was conducted according to the case-control type and includes 279 people permanently residing in the territory of the Republic of Belarus, for 68 of whom the presence of gambling addiction was established, while 211 people did not have an addiction to gambling. The comparison group according to the main demographic criteria: gender, age, social status, etc., corresponded to the main group. The study was carried out using an amplifier CFX96 Touch (Bio-Rad), HRM analysis was used for genotyping, and the results were validated using restriction analysis. The polymorphic loci whose influence on the risk of developing gambling addiction was studied by us were rs6902771 (ESR1), rs7085104 (*AS3MT*), rs7590720 (*PECR*), rs11191580 (*NT5C2*), rs56205728 (*BUB1B-PAK6*), rs7290290 (*HIP*), rs2007044 (*CACNA1C*), rs2273500 (*CHRNA4*), rs3735025 (*DGKI*), rs4356203 (*PIK3C2A*) and rs17504622.

In the course of the study, statistically significant differences between the groups were revealed when they were compared for the polymorphic loci rs17504622 (p=0.009), rs73229090 (p=0.002), rs237238 (p=0.049). Analysis for other polymorphic loci did not reveal any statistically significant differences between the groups.

MASS SPECTROMETRY APPLIED TO THE MONITORING OF ADHERENCE TO THERAPY IN CHRONIC PHARMACOLOGICAL TREATMENTS

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A poor adherence to therapy in chronic treatments has recently been reported in several pathological conditions including hypertension, dyslipidemic conditions and diabetes. This impacts severely public health and pharmacoeconomy.

The present work aims at testing the application of modern mass spectrometry in order to personalize the pharmacological therapy on the basis of the patient's adherence to the treatment, a factor often overlooked by the clinicians.

The adopted approach uses liquid chromatography hyphenated with mass spectrometry to quantitatively determine drugs and metabolites in biological fluids and hair of subjects undergoing chronic treatments with statins and antihypertensive drugs (beta-blockers, calcium antagonists, ACE inhibitors, diuretics). The analytical results have been correlated with the data of individual medicinal drugs purchase and, eventually, with the therapeutic effects and with the clinical data from the patient follow up.

The preliminary results show significant correlations between drug/metabolite concentrations in the different biological samples and the clinical outcome of the patients. These data strongly support the use of the analytical tools offered by the modern technology for an objective monitoring of adherence to therapy.

DEVELOPMENT OF POLY(LACTIC-CO-GLYCOLIC ACID)-BASED MICROPARTICLES CONTAINING RILPIVIRINE FOR LONG-ACTING HIV THERAPY

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Antiretroviral therapy adherence is crucial for the treatment of HIV infection. Development of long-acting injectable formulations (LAI) of antiretroviral drugs could improve convenience and patients' compliance. Thus, recent clinical studies demonstrated high efficacy of the nanocrystal LAI of rilpivirine and cabotegravir.

The **objective** of this study was to investigate an alternative approach to the rilpivirine LAI using the poly(lactic-co-glycolic) acid microspheres (RPV-PLGA) as drug carriers.

The optimal parameters for obtaining the RPV-PLGA microspheres using microfluidic technique (PLGA_RPV1) found in this study included employment of a 2% solution of PLGA in ethyl acetate as an organic phase and a 2% solution of polyvinyl alcohol as an aqueous phase; the flow rate ratio between the organic phase and aqueous phase was 0.15. The initial drug content was 185.2 μg/mg PLGA. Thus obtained PLGA_RPV1 microspheres had an average diameter of 45.9±4.2 μm; rilpivirine encapsulation efficiency was ~95%. The RPV-PLGA prepared by a conventional emulsification-solvent evaporation technique (PLGA_RPV2) had an average diameter of 74.7±31.3 μm; rilpivirine encapsulation efficiency was ~90%. Importantly, the microspheres prepared using different techniques demonstrated the distinct drug release profiles: the PLGA_RPV2 microspheres released the rilpivirine at a faster rate as compared to the PLGA_RPV1 (35% vs 11% during 4 weeks, respectively). The profile of rilpivirine release from the PLGA_RPV1 microspheres exhibited the near zero-order release kinetics (r^2 = 0.978) with practically no burst effect.

The **results** of the study suggest that the PLGA microspheres loaded with rilpivirine is a promising approach to the injectable depot formulation of this drug.

The reported study was funded by Russian Foundation of Basic Research, project No 20-015-00291.

DIFFERENCES IN THE PROCESSES OF ACCUMULATION, RETENTION, AND METABOLISM OF THE FLUORESCENT DYE RHODAMINE 123 IN NORMAL AND TUMOR CELLS

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Mitochondrial membrane potential (ΔΨm) is involved in a variety of cellular processes, justifying the importance of adequate ΔΨm estimation. The commonly used approach by the fluorescence intensity of dyes accumulated in mitochondria has a number of defects associated with different retention by normal and tumor cells. One possibility may be in the transformation of the original membrane-permeable into a non-permeable form.

We analyzed butanol extracts obtained after incubation of astrocytes and glioma C6 cells with rhodamine 123 (R123) using TLC and mass-spectrometry and found a cell-type-dependent modifications of R123 (e.g., formation of deesterified R123 (R110) in both cell types). In glioma cells, components with molecular weight higher than of R123 were found. When assessing the dependence of the probe retention on ΔΨm after incubation of cells with R123 and uncoupler CCCP, differences were also observed: while fluorescence vanished in astrocytes after 5h, it still retained in glioma even after 24h. Incubation with R123 and amiodarone (inhibitor of P450 and non-specific pumps), R123 derivatives were not detected in glioma extracts, suggesting the participation of P450 in the metabolism of R123 in glioma. In astrocytes, an increase of total fluorescence was observed, indicating P450-dependent processing of R123, while glioma use other ways to modify the dye.

Ultimately, covalent adducts and soluble impermeable fluorescent derivatives of R123 were found in glioma cells. No such modifications were found in astrocytes.

Given the antitumor activity of R123, this data can be used in an anti-cancer strategy.

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THE PATHOGENETIC ROLE OF INFLAMMATION IN JUVENILE SCHIZOPHRENIA

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Introduction. Inflammation is now known to be a key factor in the development of schizophrenia. In this regard, the study of the pathogenic role of inflammation in the early stages of schizophrenic process is of particular importance, making it possible to assess its activity and to predict the development of the disease.

The objective: to compare a number of inflammatory biomarkers in blood of patients with first-episode schizophrenia and in the group with signs of risk of developing schizophrenia during the treatment. Patients with juvenile depression with attenuated symptoms of schizophrenic spectrum (ASSS) were investigated as a risk group.

Materials and methods. Twenty patients aged 17 to 25 years were examined, of which 10 patients with first-episode schizophrenia (F20.0 for ICD-10) and 10 ones with juvenile depression with ASSS (F32.1, F32.2, F32.38, F32.8). The control group consisted of 10 mentally healthy volunteers comparable in age to patients (mean age 20.4 ± 1.6 years). Patients were examined at admission to the hospital and at discharge. Psychopathological, psychometric (PANSS, SOPS, SANS, HDRS scales), immunological (medical technology "Neuroimmunotest") and statistical methods were used. The level/activity of inflammation markers was determined in blood plasma: tumor necrosis factor-α, interleukin-6 (IL-6), interleukin-10 (IL-10), leukocyte elastase (LE), C-reactive protein (CRP) and α1-proteinase inhibitor (α1-PI). The levels of antibodies to S100-β and MBP were also estimated.

Results. An increase in the level/activity of a number of inflammatory markers in both patient groups compared to control was found ($p<0.05$). The highest values of indicators, including IL-6, LE, CRP, α1-PI and antibodies to S100-β in patients with first-episode schizophrenia were revealed ($p=0.03$). Thus, the active stage of the disease was characterized by the activation of systemic inflammatory reactions, including the autoimmune component to neuroantigens. After the treatment, the positive trend of inflammatory markers in patients with first-episode schizophrenia was detected ($p<0.05$); no significant changes in indicators were observed in patients with juvenile depression with ASSS (except LE activity, $p<0.05$).

Conclusions. The results obtained confirm the pathogenic role of inflammation in the pathogenesis of endogenous mental disorders. It can be assumed that the level of inflammatory biomarkers studied reflects the activity of the current pathological process in the early stages of schizophrenia.

ЭЛЕКТРОННЫЙ ПАРАМАГНИТНЫЙ РЕЗОНАНС В ИССЛЕДОВАНИИ БИОДЕГРАДАЦИИ 3Х МЕРНЫХ СТРУКТУР

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Синтетические полимеры на основе алифатических полиэфиров, разлагающиеся в организме за времена от нескольких недель до нескольких месяцев с образованием низкотоксичных молочной и гликолиевой кислот, являются перспективными материалами для изготовления временных протезов различных тканей и органов (матриксов, 3d структур). Полимер может быть допирован биологически активными веществами — противовоспалительными, противоопухолевыми и др., которые по мере разложения временного протеза высвобождаются в организм. Кинетика высвобождения допантов определяется механизмом гидролитической деградации полимера, архитектоникой образца, а также распределением допанта в полимерной матрице. Использование парамагнитных добавок, в том числе спин-меченых биологически активных соединений, открывает широкие возможности для диагностики полученных материалов и установления кинетических закономерностей их гидролитической деградации методом электронного парамагнитного резонанса (ЭПР).

В докладе будут представлены результаты исследования полимерных форм из D,L-полилактида (пористых матриксов и пленок) методом ЭПР в рамках методики спинового зонда. В качестве зондов использованы стабильные нитроксильные радикалы TEMPOL, TEMPONE, pH-чувствительные зонды и спин-меченые биологически активные вещества.

Данный подход позволил оценить равномерность распределения допанта в матриксах на макроскопическом и молекулярном уровнях, установить кинетические закономерности высвобождения биологически активного соединения в водную среду *in vitro*, характеризовать изменение полярности и pH во внутренней среде полимерного материала, и, в результате, сформулировать механизм гидролитической деградации алифатических полиэфиров.

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