Biomeditsinskaya Khimiya

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

2017 volume 63 issue 5

1. Moshkovskii S.A.

Omics biomarkers and early diagnostics.

One of main goals for omics sciences, such as transcriptomics, proteomics and metabolomics, in medicine is biomarker discovery for diagnostics of common non-infectious diseases. The opinion paper discusses diagnostic parameters, which limit the use of the biomarkers, as well as a positive predictive value, and conditions providing possible application of the biomarkers for early diagnostics. Using some examples from proteomics, it is stated that omics technologies, which measure gene expression products, are more often used to discover prognostic and predictive biomarkers. These biomarkers help to classify already diagnosed patients to groups with different disease management.

DOI: 10.18097/PBMC20176305369

2. Poverennaya E.V., Kiseleva O.I., Ponomarenko E.A., Naryzhny S.N., Zgoda V.G., Lisitsa A.V.

Multiomics study of HepG2 cell line proteome.

Current proteomic studies are generally focused on the most abundant proteoforms encoded by canonical nucleic sequences. Transcriptomic and proteomic data, accumulated in a variety of postgenome sources and coupled with state-of-art analytical technologies, allow to start the identification of aberrant (non-canonical) proteoforms. The main sources of aberrant proteoforms are alternative splicing, single nucleotide polymorphism, and post-translational modifications. The aim of this work was to estimate the heterogeneity of HepG2 proteome. We suggested multiomics approach, which combines transcriptomic (RNAseq) and proteomic (2DE-MS/MS) methods, as a promising strategy to explore the proteome.

DOI: 10.18097/PBMC20176305373

3. Sergeeva V.A., Muminova K.T., Starodubtseva N.L., Kononikhin A.S., Bugrova A.E., Indeykina M.I., Baibakova V.V., Khodzhaeva Z.S., Kan N.E., Frankevich V.E., Shmakov R.G., Nikolaev E.N., Sukhikh G.T.

Features of the urine peptidome under the condition of hypertensive pathologies of pregnancy.

In order to find a peptide panel to differentiate close hypertensive conditions a case-control study was designed for 64 women from 4 groups: preeclampsia (PE), chronic hypertension superimposed with PE, chronic hypertension, and healthy individuals. Chromatography coupled with mass-spectrometry and subsequent bioinformatic analysis showed several patterns in the changes of the urine peptidome. There were 36 peptides common for four groups. Twenty two of them 22 belonged to alpha-1-chain of collagen I, nine peptides were from alpha-1-chain of collagen III, two from alpha-2-chain of collagen I, one from alpha-1/2-chain of collagen I, one from alpha-1-chain of collagen I/XVIII and one from uromodulin. Patients with hypertensive disorders had 34 common peptides: 12 from alpha-1-chain of collagen I, 10 from fibrinogen alpha-chain, eight from alpha-1-chain of collagen III, and 4 per other types of collagen. Comparative analysis revealed 12 peptides, which could be used as a diagnostic panel for confident discrimination of pregnant women with various hypertensive disorders.

DOI: 10.18097/PBMC20176305379

4. Zorina I.M., Eldarov C.M., Yarigina S.A., Makarova N.P., Trofimov D.Yu., Smolnikova V.Yu., Kalinina E.A., Bobrov M.Yu.

Metabolomic profiling in culture media of day-5 human embryos.

The aim of this study was to determine the changes of metabolomic profiles in embryonic culture media (ECM) for the evaluation of quality and implantation potential of human embryos. ECM (n=163) were collected on day 5 before transfer or cryopreservation. Some embryos were used in preimplantation genetic screening for detection of aneuploidy karyotypes. Samples were subdivided into groups according to embryo morphological classification (by Gardner), genetic analysis and implantation data. ECM were extracted with methanol, precipitates were separated by centrifugation and metabolite production of individual embryo was analysed by LC-MS (the positive ion mode). After peak detection and retention time alignment, data were analysed using the PCA algorithm. MS fingerprinting analysis of embryo culture medium showed significant differences between morphologically divided groups. Intragroup comparisons did not reveal differences between subclasses. Genetic screening of embryos revealed 33 aneuploid karyotypes. It was shown that chromosome number did not affect the metabolite profiles comparing with the normal group. The culture media of embryos that were positive or negative for successful implantation showed specific signatures that allowed to distinguish embryos with different outcomes.The characterization of ECMs by LC-MS may facilitate more accurate selection of the best embryo for the implantation, improving single-embryo transfer and thus eliminating the risk and undesirable effects of multiple pregnancies.

DOI: 10.18097/PBMC20176305385

5. Ponomareva J.V., Limareva L.V., Milyakova M.N.

The range and potential contribution of irreversibly adsorbed proteins on the surface of artificial implants.

Protein adsorption is the first stage of the interaction between prosthetic materials with tissues of the body. They undergo conformational changes depending on the chemical composition and the nanotopography surface. Adsorbed proteins induce adhesion and alter the functional state of migrating cells. Plasma samples from patients were incubated with such matrices as titanium, polypropylene or polyester with fluoropolymer coating meshes. Bound peptides were analyzed by electrophoresis. Qualitative analysis of the peptides extracted from the gel was performed by chromatography-mass spectrometry. Quantitative analysis was performed by the MRM method. More than 60 proteins were identified on the analyzed surfaces. Quantitative

analysis showed preferential adsorption of vitronectin, albumin, fibrinogen a-chain, C1Ñ• component of the complement system. Vitronectin had the maximum relative protein content. Since biocompatibility of the analyzed materials varies considerably this variability may be attributed to conformational changes occurring with vitronectin during its irreversible adsorption.
DOI: 10.18097/PBMC20176305392

6. Mikurova A.V., Novikova S.E., Skvortsov V.S., Alekseychuk N.N., Rybina A.V., Miroshnichenko Yu.V.

The sequence coverage in different methods of mass spectrometry data analysis obtained on model proteins.

The aim of this study was to evaluate sequence coverage of five model proteins (CYB5A, SMAD4, RAB27B, FECH, and CXXC1) by means of shotgun proteomic data analysis employing different methods of data treatment including database-dependent search engines (MASCOT and X!Tandem) and de novo sequencing software ((PEAKS, Novor, and PepNovo+). In order to achieve maximal results, multiprotease hydrolysis including enzymes trypsin, LYS-C, ASPN and GluC was performed in solution and using the FASP method. High resolution mass spectrometry was carried out with a Q EXACTIVE HF hybrid mass spectrometer in the positive ionization mode; parent ions with the highest intensity and a charge range from +2 to +6 were fragmented in the HCD mode. 27 experiments were carried out (hydrolysis with each of 5 enzymes in solution, 4 for the FASP protocol, three technical repeats). Using parameters limiting false identification of peptides, the search engines and de novo sequencing software gave similar results. The degree of sequence coverage was not at least 40%, and in the best cases it reached 80-90%. The use of de novo sequencing software resulted in identification of the Y12H amino acid substitution in one model protein (CYB5A).
DOI: 10.18097/PBMC20176305397

7. Rusanov A.L., Petushkova N.A., Poverennaya E.V., Nakhod K.V., Larina O.V., Lisitsa A.V., Luzgina N.G.

Proteomic profiling of HaCaT keratinocytes exposed to skin damaging detergents.

The effects of sodium dodecyl sulfate (25 mg/ml) and Triton X-100 (12.5 mg/ml and 25 mg/ml) on the HaCaT immortalized keratinocytes exposed to these surfactants for 48 h were studied. Using shotgun proteomics, a comparative analysis of the proteomic profiles of control and experimental cells after surfactants exposure was carried out. 260 common proteins were identified in control and experimental cells; 33 proteins were found in cells exposed to all three treatments, but not in control cells. These 33 proteins apparently reflect a nonspecific (universal) response of cells to toxic damage by the surfactants. These proteins are associated with activation of cell proliferation, changes in the functional activity of their ER and mitochondria, increased mRNA stability and activation of protein degradation processes in the cells. The possibility of using these proteins as a nonspecific parameter of cell response to cytotoxic damage is discussed. The mass spectrometry proteomics data (â€œrawâ€•, â€œmgfâ€• and â€œxmlâ€• files) have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifiers PXD007789 and PXD007776.
DOI: 10.18097/PBMC20176305405

8. Tsukanov K.Yu., Krasnenko A.Yu., Plakhina D.A., Korostin D.O., Churov A.V., Druzhilovskaya O.S., Rebrikov D.V., Ilinsky V.V.

A bioinformatic pipeline for NGS data analysis and mutation calling in human solid tumors.

We aimed to develop a pipeline for the bioinformatic analysis and interpretation of NGS data and detection of a wide range of single-nucleotide somatic mutations within tumor DNA. Initially, the NGS reads were submitted to a quality control check by the Cutadapt program. Low-quality 3Â¢-nucleotides were removed. After that the reads were mapped to the reference genome hg19 (GRCh37.p13) by BWA. The SAMtools program was used for exclusion of duplicates. MuTect was used for SNV calling. The functional effect of SNVs was evaluated using the algorithm, including annotation and evaluation of SNV pathogenicity by SnpEff and analysis of such databases as COSMIC, dbNSFP, Clinvar, and OMIM. The effect of SNV on the protein function was estimated by SIFT and PolyPhen2. Mutation frequencies were obtained from 1000 Genomes and ExAC projects, as well as from our own databases with frequency data. In order to evaluate the pipeline we used 18 breast cancer tumor biopsies. The MYbaits Onconome KL v1.5 Panel (â€œMYcroarrayâ€•) was used for targeted enrichment. NGS was performed on the Illumina HiSeq 2500 platform. As a result, we identified alterations in BRCA1, BRCA2, ATM, CDH1, CHEK2, TP53 genes that affected the sequence of encoded proteins. Our pipeline can be used for effective search and annotation of tumor SNVs. In this study, for the first time, we have tested this pipeline for NGS data analysis of samples from patients of the Russian population. However, further confirmation of efficiency and accuracy of the pipeline is required on NGS data from larger datasets as well as data from several types of solid tumors.
DOI: 10.18097/PBMC20176305413

9. Orlov Y.L., Thierry O., Bogomolov A.G., Tsukanov A.V., Kulakova E.V., Galieva E.R., Bragin A.O., Li G.

Computer methods of analysis of chromosome contacts in the cell nucleus based on sequencing technology data.

The study spatial chromosome structure and chromosome folding in the interphase cell nucleus is an important challenge of world science. Detection of eukaryotic genome regions that physically interact with each other could be done by modern sequencing technologies. A basic method of chromosome folding by total sequencing of contacting DNA fragments is HI-C. Long-range chromosomal interactions play an important role in gene transcription and regulation. The study of chromosome interactions, 3D (three-dimensional) genome structure and its effect on gene transcription allows revealing fundamental biological processes from a viewpoint of structural regulation and are important for cancer research. The technique of chromatin immunoprecipitation and subsequent sequencing (ChIP-seq) make possible to determine binding sites of transcription factors that regulate expression of eukaryotic genes; genome transcription factors binding maps have been. The ChIA-PET technology allows exploring not only target protein binding sites, but also pairs of such sites on proximally located and interacting with each other chromosomes co-located in three-dimensional space of the cell nucleus. Here we discuss the principles of the construction of genomic maps and matrices of chromosome contacts according to ChIA-PET and Hi-C data that capture the chromosome conformation and overview existing software for 3D genome analysis including in house programs of gene location analysis in topological domains.
DOI: 10.18097/PBMC20176305418

10. Karasev D.A., Savosina P.I., Sobolev B.N., Filimonov D.A., Lagunin A.A.

Application of molecular descriptors for recognition of phosphorylation sites in amino acid sequences.

Recognition of the phosphorylation sites in proteins is required for reconstruction of regulatory processes in living systems. This task is complicated because the phosphorylation motifs in amino acid sequences are considerably degenerated. To improve the prediction efficacy researchers often use additional descriptors, which should reflect physicochemical features of site-surrounding regions. We have evaluated the reasonability of this approach by applying molecular descriptors (MNA) for structural presentation of the peptide segments. Comparative testing was performed using the prognostic method PASS and two input data types: sets of the MNA descriptors represented peptides as chemical structures and amino acid sequences written using a one-letter code. Training sets were classified in accordance with the established types of the enzymes (protein kinases), modifying corresponding phosphorylation sites. The accuracy estimates obtained by prognosis validation for various classes of substrates were significantly different with both the letters and molecular descriptors. In case of the letter description, the prognosis accuracy demonstrated less dependence on the length of peptides in the training set, while in the case of structural descriptors the accuracy level was determined by the peptide size and descriptor characteristics (MNA levels). The maximal prognosis accuracy related to various kinase families was achieved at different sizes of molecular fragments covered by the MNA descriptors of corresponding levels. This obviously reflected structural differences in surroundings of phosphorylation sites modified by various protein kinases. The use of molecular descriptors provided the prognostic results comparable with the results obtained using traditional letter representation. The prognosis accuracy demonstrated less dependence on the method describing site-surrounding peptides at higher accuracy rates. Applying the MNA descriptors it is possible to achieve better accuracy in the cases when the letter description cannot provide acceptable accuracy.

DOI: 10.18097/PBMC20176305423

11. Sazanov A.A., Erganokov Kh.Kh., Pfeifer E.

A cryobank as an attribute of omics technologies.

Biobanks are systematic and annotated collections of biological samples based on the system of standard operating procedures (SOP) and corresponding to the recommendations of the International Society for Biological and Environmental Repositories (ISBER). Standardization of conditions of obtaining, processing, storage of samples and providing to an end user are crucial in the activities of the biobank. The attributes of biobanks include common principles of labeling and annotation of biological samples using specialized software, an automated monitoring system of storage conditions, and registration of biosamples. Cryobanks are the biobanks maintained at the storage conditions from -196Â°C to -150Â°C that provide better cell viability and the highest preservation of biological molecules. Cryobanking is the most essential part of the infrastructure of population and personalized medicine, pharmaceuticals and biopharmacology, conservation of rare and endangered species, as well as biotechnology in general. Next Generation Biobanking, a concept especially designed for omics technologies, involves annotating biological samples on many biomarkers based on Next Generation Sequencing techniques, as well as collecting biological material from the same patient at different time points (for example, at different stages of the disease, before and after the operation, at different periods of therapy) with a detailed annotation of physiological, biochemical and clinical data. Epigenetic studies (DNA methylation, microRNA, etc.), as well as bioinformatic data analysis are of great importance in the activity of Next Generation Biobanking. Such biobanks should function based on the new ethical principles of the post-genomic era.

DOI: 10.18097/PBMC20176305428

12. Sychev D.A., Shih N.V., Kalle E.G., Ryzhikova K.A., Morozova T.E.

Pharmacogenetic approaches to predicting the efficiency and safety of amlodipine in patients with arterial hypertension.

An open, non-comparative, prospective clinical study was conducted to evaluate the antihypertensive efficacy and tolerability of amlodipine, a calcium antagonist, in patients with arterial hypertension (AH) I-II stages, depending on the genotype for the polymorphic marker C3435T of the ABCB1 gene. The study included 100 patients with AH I-II stages, aged from 45 to 58 years. The initial dose of amlodipine was 5 mg, duration of treatment was 12 weeks. General clinical examination methods, office measurement and daily blood pressure monitoring, tolerance evaluation, and genotyping using the ABCB1 polymorphic marker C3435T by the PCR-RFLP method (polymerase chain reaction and restriction fragment length polymorphism) were used. The statistical analysis of results was carried out using the Mann-Whitney U test for quantitative variables, Kruskal-Wallis one-way analysis of variance (ANOVA) for three independent groups of quantitative data. Excellent antihypertensive efficacy with the CC genotype was found in 11.8% patients, with CT â€“ 33.9%, with TT â€“ 43.3%; good â€“ 35.3%, 32.1%, and 33.3% respectively, satisfactory â€“ 52.9%, 34,0% and 23.4% respectively. Six patients with the CT genotype and nine patients with the CC genotype required the increase in the dose to 10 mg. The number of patients with Adverse drug reactions (ADR) were found in 35.3% of patients with the CC genotype, 6.7% with the TT genotype and 11.3% with the CT genotype. The Kruskal-Wallis test revealed significant differences between CC and TT genotypes in the degree of decrease in SBP (p=0.02), antihypertensive efficacy parameter (p=0.02), an increase in dose requirements (p = 0.04) and the incidence of ADR(p=0.05). In AH patients (I-II stage) with the TT genotype of the C3435T gene polymorphism one can expect higher rates of antihypertensive efficacy of amlodipine in combination with a good safety profile and the lowest ADR percentage, while patients with the CC genotype more likely to develop ADR and lower antihypertensive responsiveness.

DOI: 10.18097/PBMC20176305432

13. Gal`perin E.I., Ataullakhanov R.I., Dyuzheva T.G., Platonova L.V., Melnikova T.M., Monakov M.Yu., Dudchenko A.M., Lyundup A.V., Klabukov I.D.

Possible use of the growing liver biological set for hepatic recovery after toxic damage (an experimental study).

The lack of acceptable pharmacological approaches for restoration of the injured liver is associated with complex of mechanisms involved in hepatic regeneration and with difficulty of the target selection. The aim of this research was to study the hepatoprotective function of the extract from both the growing and regenerating liver containing a natural set of factors crucial for the hepatic restoration. Extracts from both regenerating liver of rats after 70% hepatic resection and the growing liver of neonatal pigs were obtained using own original technique. The set of resultant extracts was named as the hepatic regeneration set (HRS). HRS fractionation was carried out using the Toyopearl HW-50S sorbent. The efficiency of HRS and its fractions was estimated using a model of the mouse liver thioacetamide injury and monitoring hepatic enzyme activity in blood serum. The activities of AST and ALT in intact animals were 50 U/l and 80 U/l, respectively; after thioacetamide administration they increased to 2059Â±212 U/l and 4280Â±440 E/l,

respectively (p<0.05). Treatment of injured animals with HRS from the rat regenerating liver resulted in a significant decrease of transaminase activities to 924Â±148 U/l (AST; p<0.05) and 1633Â±308 U/l (ALT; p<0.05). A similar effect was observed after treatment with HRS from the neonatal pig liver: the AST decreased to 937Â±138 U/l (p<0.05), while ALT activity decreased to 1710Â±237 U/l (p<0.05). HRs fractionation resulted in identification two active fractions characterized by much higher (8-29) hepatotropic effect that that of the whole extract. These fractions contained peptide/protein components with the range of molecular mass of 3-60 kDa (fraction 1) and 3-25 kDa (fraction 2a). Fraction 1 also contained some polynucleotides in fraction 1. Subsequent studies of these fractions exceeding the hepatotropic effect of original HRS is clearly needed to identify their individual components by immunochromatography methods, ELISA, MRM mass spectrometry and quantitative PCR.
DOI: 10.18097/PBMC20176305440

14. Berdugina O.V., Berdugin K.A.

Changes in laboratory parameters of peripheral blood reflect cell and protein content of the immune system in bone resorption.

The aim of this study was to investigate dynamic changes in the laboratory parameters of peripheral blood, reflecting cellular and protein composition of the immune system in bone resorption. The study involved 108 patients with degenerative-dystrophic and posttraumatic disorders of the hip joint before and after joint replacement surgery. Half of the cases resulted in bone resorption. Dynamic monitoring was performed up to 7.5 years. It included flow cytometry (Coulter Epics XL, USA) and enzyme immunoassay to determine the amount of immunocompetent cells, immunoglobulin class M, A, G, E, cytokines, acute phase proteins (C-reactive protein, fibrinogen, albumin, ceruloplasmin, haptoglobin), parameters of neutrophil functional activity (lactoferrin cationic protein, myeloperoxidase, superoxide anion production). The results of the study revealed the leading role of haptoglobin, albumin, and IL-1b in bone resorption. The use of multiple regression analysis made it possible to propose criteria for prediction of bone resorption. In particular, the Ig G concentration one month after operation at a value of 13 or less g/l with a probability of 86.8% suggests a high risk of bone tissue destruction in the operated area of the joint (diagnostic sensitivity and diagnostic specificity of 85.7% and 86.9%, respectively). Determination of the IL-1b level also has a good predictive power: its concentration exceeding 191.2 pg/ml six month after surgery with the probability of 87.4% suggests destruction of bone tissue in the operated area of the joint (diagnostic sensitivity and diagnostic specificity of 87.2% and 88.1%, respectively).
DOI: 10.18097/PBMC20176305447

15. Sokolova M.G., Lobzin S.V., Penniyaynen V.A., Kipenko A.V., Lopatina E.V., Rezvantsev M.V., Gavrichenko A.V.

The role of polypeptide compounds in mechanism of CNS plasticity in patients with hereditary pathology of peripheral motor neuron.

Synaptic pruning is a physiological mechanism of neuroplasticity, which is regulated through synthesis of growth polypeptides, neurotrophins. The role of neurotrophins in the mechanism of synaptic pruning in patients with hereditary pathology of peripheral motor neuron was studied in a clinical experimental trial. It was found that patients had elevated levels of regulatory growth polypeptides, which led to the axon growth inhibition effect in organotypic tissue cultures. Thus, neurotrophin overexpression can be considered as a factor preventing synaptic pruning and contributing to further process of neurological degeneration in nerve tissue in patients with hereditary pathology of peripheral motor neuron.
DOI: 10.18097/PBMC20176305453

16. Tarasova O.A., Filimonov D.A., Poroikov V.V.

Computational prediction of human immunodeficiency resistance to reverse transcriptase inhibitors.

Human immunodeficiency virus (HIV) causes acquired immunodeficiency syndrome (AIDS) and leads to over one million of deaths annually. Highly active antiretroviral treatment (HAART) is a gold standard in the HIV/AIDS therapy. Nucleoside and non-nucleoside inhibitors of HIV reverse transcriptase (RT) are important component of HAART, but their effect depends on the HIV susceptibility/resistance. HIV resistance mainly occurs due to mutations leading to conformational changes in the three-dimensional structure of HIV RT. The aim of our work was to develop and test a computational method for prediction of HIV resistance associated with the mutations in HIV RT. Earlier we have developed a method for prediction of HIV type 1 (HIV-1) resistance; it is based on the usage of position-specific descriptors. These descriptors are generated using the particular amino acid residue and its position; the position of certain residue is determined in a multiple alignment. The training set consisted of more than 1900 sequences of HIV RT from the Stanford HIV Drug Resistance database; for these HIV RT variants experimental data on their resistance to ten inhibitors are presented. Balanced accuracy of prediction varies from 80% to 99% depending on the method of classification (support vector machine, Naive Bayes, random forest, convolutional neural networks) and the drug, resistance to which is obtained. Maximal balanced accuracy was obtained for prediction of resistance to zidovudine, stavudine, didanosine and efavirenz by the random forest classifier. Average accuracy of prediction is 89%.
DOI: 10.18097/PBMC20176305457

17. Tillib S.V., Morgunova E.Y., Ivanova T.I., Koroleva E.A., Rutovskaya M.V., Zigangirova N.A.

Single-domain adapted antibodies against Chlamydia trachomatis, preserving the development of chlamidic infection in vitro.

The technology for the generating of single-domain recombinant monoclonal antibodies (nanoantibodies) based on the immunization of a camel, cloning of induced sequences encoding single-domain antigen-recognizing fragments of non-canonical camel antibodies, as well as functional selection of clones of nanoantibodies by the phage display method, was used to obtain new effective tools for more efficient diagnostics of Chlamydia infection and to develop new approaches for effective therapy. Two promising nanoantibodies were obtained. They showed effective binding to extracellular and intracellular forms of C. trachomatis, and also had activity that inhibited the development of chlamydial infection in vitro.
DOI: 10.18097/PBMC20176305461

18. Nosova A.S., Koloskova O.O., Shilovskiy I.P., Sebyakin Yu.L., Khaitov M.R.

Lactose-based glycoconjugates with variable spacers for design of liver-targeted liposomes.

Asialoglycoprotein receptors are highly abundant on the hepatocyte surface and have specific binding sites for blood serum glycoproteins. Such discovery resulted in development of liver-targeted drug delivery systems because modification of the liposomal surface by carbohydrate derivatives

results in an increase of endocytosis, which facilitates selective uptake of such systems by hepatocytes. In this study we have synthesized novel lactose derivatives containing a palmitic hydrophobic domain. They were used for modification of the liposome surface. Transfection activity of modified liposomes was analyzed on the HepG2 cell line (hepatocytes) and showed an increase in the transfection efficiency as compared to the non-modified liposomes. At the same time transfection activities of modified and non-modified liposomes were similar in the case of a non-hepatocyte cell line (293T). The novel lactose-based glycoconjugates may be a promising tool for developing efficient vectors for delivery of nucleic acids to hepatocytes.
DOI: 10.18097/PBMC20176305467

19. Turetskiy E.A., Koloskova O.O., Nosova A.S., Shilovskiy I.P., Sebyakin Yu.L., Khaitov M.R.

Physicochemical properties of lipopeptide-based liposomes and their complexes with siRNA.

siRNA/cationic liposome complexes are efficient systems for transmembrane delivery. The aim of this study was to prepare a novel complex consisted of lipotripeptide OrnOrnGlu(C16H33)2 and siRNA molecule and examined their physicochemical properties. Electron microscopy study has shown that the siRNA/liposome complex (m/m 1/10) tends to form sandwich-like structures that may protect nucleic acid from nuclease degradation. Photon correlation spectroscopy data indicate that the particle size increased after siRNA adding, but did not exceed 300 nm in diameter, while z-potential of lipoplexes decreased from 22 mV to 14 mV, compared to the empty liposomes thus indicating positive charge neutralization by negatively charged siRNA. These data allow to hypothesize that such size and total positive charge could provide efficient cellular uptake by endocytosis. That may have good prospects for gene silencing therapy.
DOI: 10.18097/PBMC20176305472