Research Article

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Possibilities of Multi-Omiks Technologies in Personalized Medicine

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ABSTRACT

In this paper, we discuss the role of multi-omiks technologies in modern biomedicine and development concept of personalized medicine. There are some preliminary results of the investigation of the metallom. It was shown that the stable level of components metallom is the most important factor of cellular homeostasis and individual elementogramma is a dynamic indicator of metalloligand homeostasis – MLH. It is established that the use of results of omiks technology - elementogramms may be necessary for both pre-nosological diagnosis and for subsequent planning of individual treatment and prevention of pathology associated with metabolic disorders.

Keywords

Omiks technologies, Personalized medicine, Metabolom, Metallom, metabonom, Individual elementogramma, Trace elements.

Actuality

Medicine of XXI century is inextricably linked, and increasingly uses data omiks technologies for the diagnosis and treatment of various diseases. The use of multiomic technology in biomedicine contributes to the formation of an innovative concept of individual approach to each patient, i.e. personalized medicine.

The appearance of personalized medicine the basic principle of which is selection treatment of methods according to the genetic characteristics patients and their pathologically altered cells stimulated increasing flow of genetic data and diagnostic approaches which began with the human genome. Even before subject of attention in medicine became concept of personalization and individual approach was applied, for example, in blood transfusion, tissue transplantation, cell therapy, as well as in the selection of drugs and dietary supplements for correction of metabolic disorders. Individualization of treatment is implied in genomic medicine as a pre-symptomatic identification of a predisposition to a particular disease, preventive measures and choice of pharmacotherapy and individual selection of treatment regimens carried out on the basis of genotype determination. Genotyping is an important basis, but in the development of personalized medicine, other omix technologies are also used such as study of metabolom, metabonom, metallom, etc..

Metabolomics is a "systematic study of unique chemical" fingerprints "specific for processes occurring in living cells" - more specifically study of their low-molecular metabolic profiles [1]. Metabolom is represent of all metabolites which are the final product of metabolism in a cell, tissue, organ or organism [2], which can be found both in a biological sample and in a single organism [3-4]. In January 2007, scientists from the University of Alberta and the University of Calgary completed the first version of the human metabolom. They cataloged about 2500 metabolites, 1200 medicines and 3500 food components that can be found in the human body [5]. This information, available in the human metabolic database (www.hmdb.ca) and based on the analysis of existing scientific literature is not complete. About metaboloms of other organisms are known more. For example, more than 50,000 plant metabolites have been identified; many thousands have been identified and characterized in single plants [6-7].

Metabonomics is defined as the "quantitative measurement of the dynamic multiparameter metabolic response of living systems to pathophysiological effects or gene modifications". The term comes from the Greek meta meaning "change", and nomos, meaning "set of rules or patterns" [8]. This approach was first proposed and used by Jeremy Nicholson at the Royal College of London and used in toxicology, diagnosis of diseases and a number of other areas. Historically, the metabonomic approach was one of the first attempts to use techniques systemic biology for study of metabolism [9-11].

Metallomics is a quantitative measurement component of metallom -products interaction of ionic and atomic forms of metals with endogenous ligands (nucleotides, nucleosides, proteins, peptides, amino acids, carbohydrates, etc.). Recently, the concepts of metallomics include not only study metals in the body, but many vital chemical elements [12-14].

Currently, the role of many macro- and microelements (ME) in the growth, differentiation, regeneration, apoptosis and necrosis of cells has been established, as well as in the pathogenesis number of diseases, which is accompanied by significant changes in the elemental status of the organism. ME imbalance can indirectly become a triggering mechanism for disturbing regulation of apoptosis. The aggravating effect on manifestation of genotoxic effect number of metals is exerted deficiency and excess or imbalance number of essential ME.

The results of many years research have shown that unidirectional change in the ratio of strictly defined elements is observed in a number of pathological processes, but different in absolute magnitude. This change in elemental status is indicated by N. Kaletina with co-authors [13] as the primary (or preliminary) stressor elementogramma.

Against the background of existing stressor elementogramma, patients with clinically established diagnosis appeared additional changes in elemental status which characterized particular disease and which are called the "specific elementogramma". According to the results, a specific elementogramma can be an additional non-invasive diagnostic and prognostic test. The change in the absolute indices of the stressor and specific elementogramms is caused by many factors, including genetic, ecological, nutrition, treatment regimen, etc.

The Aim of Study

The purpose of this study was to determine the content of metallom components, ie macro-, microelements in human hair and detect deviation and analyze the possibilities of personalized approach for each patient on the basis of revealed regularities change metallom in their bodies.

Methods and Materials of Research

The Study was conducted by the method of atomic emission spectrometry with inductively coupled argon plasma (ICP-AES) and mass spectrometry with inductively coupled plasma (ICP-MS), which are highly sensitive and allow rapid and reliable determination of the level of micro- and ultra microelements. By using two complementary methods for the determination of the metallom in one biosample, reliability of the results increases and set of quantifiable elements increases and the total time spent for analysis decrease.

The object of research was the hair of people aged 20-45 years of both sexes, not engaged in industry and harmful working conditions. Hair analysis has a number of advantages: highly informative, non-invasive, easily transport and storage of samples, etc. Determining the content of chemical elements in hair allows also assessing the influence of ecological-hygienic and physiological factors on the body. The method is characterized by high information content, performance, sensitivity, and allows to identify simultaneously more than 25 chemical elements in the investigated objects (Aluminum (Al), Beryllium (Be) Boron (B), Vanadium (V), Iron (Fe), Iodine (I), Potassium (K), Cadmium (Cd) Calcium (Ca), Cobalt (Co), Silicon (Si), Lithium (Li), Magnesium (Mg), Manganese (Mn), Copper (Cu), Arsenic (As), Sodium (Na), Nickel (Ni), Tin (Sn), Mercury (Hg), Lead (Pb), Selenium (Se), Phosphorus (P), Chromium (Cr), Zinc (Zn)).

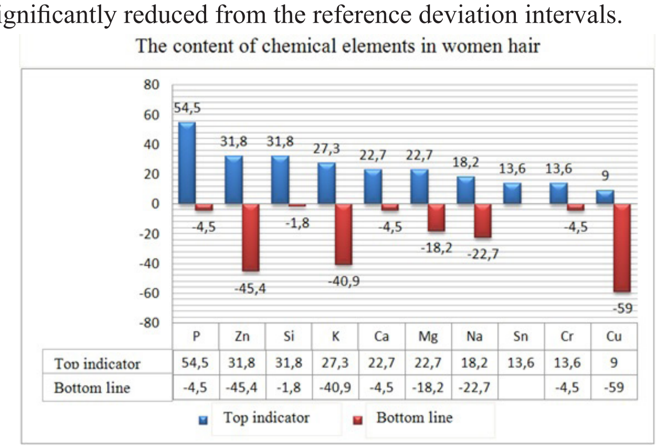
Selection and Preparation of Samples

Hair was cut from the occipital part of the head for the entire length in an amount not less than 0.1 g. To remove surface contamination and degrease hair was used method of preparing hair samples, recommended by IAEA. For this purpose, the hair treated with acetone for 10-15 minutes and then washed with distilled water three times. Hair drying will be performed at room temperature for 10-15 minutes.

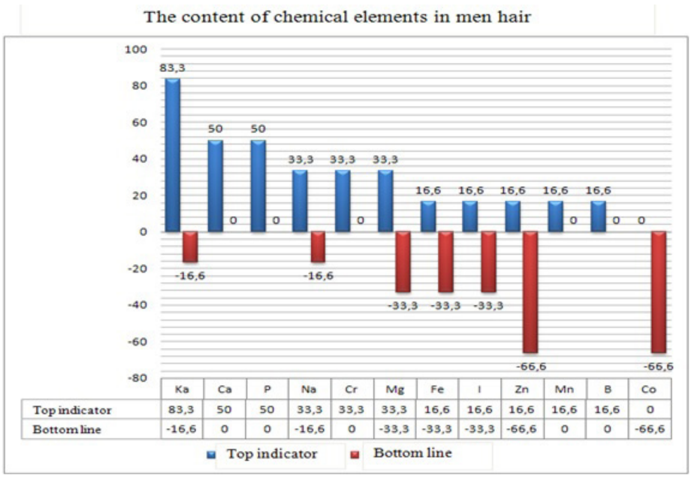
Research Results

The results of study on content of chemical elements in the hair (elementogramma) were in majority within the reference deviation intervals. The case of a significant deviation from the norm was multidirectional nature both for certain vital chemical elements and for their deficiency or excess, as might be expected. For a more reliable and adequate interpretation of the results, we carried out differentiation of the data for men and women in table1 and table 2.

As can be seen from Table 1, in women hair, the level of phosphorus, zinc, silicon, calcium, magnesium, , sodium, tin and chromium is significantly higher than that of zinc, copper and potassium significantly reduced from the reference deviation intervals.



In organism of men (Table 2), we find an increased content of chemical elements potassium, calcium, phosphorus, sodium, chromium, magnesium, and boron and reduced content of cobalt, zinc, magnesium, iron and iodine. It should be noted that the content of calcium, potassium, sodium, phosphorus, chromium and magnesium was above the norm by 25-75% in all studied population groups. More specific were deviations from the norm, that is, an increased content of essential microelements 40-50%, such as zinc and silicon in the body only in women. Particular attention is drawn to the deficiency in organisms of both groups studied by 30-70% cobalt, copper, zinc, iodine and potassium.



Discussion of Results and Conclusions

Element graph of hair of every patient shows individual elemental status – the status of the components of "metallome". Elemental composition of hair reflects the regional specificity of natural environments, due in large part to the prolonged influence of technogenic and nutritional factors. We did not pay much attention to changes in the content in the hair calcium, phosphorus, potassium, sodium and magnesium, as this may be related to age, lifestyle, social status, nutrition, and is usually short-lived. Also, we did not analyze a significant imbalance of iron, chromium, lead, manganese and boron at this stage of the study for the following reasons: first, the deviations are not reliable, and secondly need analysis content of these elements in blood, urine and specific biopsy samples. Unidirectional changes in content essential elements of copper, zinc, iodine and potassium in direction of lack, especially a significant reduction in the level of cobalt (65-73%) may indicate abnormal metabolic disorders and violation of intracellular homeostasis and a pool of metallom. Permanent and long-term disturbances of stable level metallom, especially vital irreplaceable trace elements are worrying signal for a complex study and can serve as an indicator test for detecting molecular pathology and orphan disease.

So, for example, in the human body, copper affects the activity of more than 30 enzymes, stimulates cellular respiration, the production of female sex hormones and thyroxine. Copper ions facilitate the process of transmission excitation in the brain. At intrauterine deficiency of copper can develop heart defects. There are a number of genetic diseases which violation of copper metabolism leads to damage of brain, liver, musculoskeletal system, hair, central nervous system (Konovalov-Wilson disease, Menkes disease, multiple sclerosis). The metabolism of copper is closely related to the zinc metabolism. Zinc activates about 200 different enzymes. Zinc deficiency is characterized by decreased appetite, anemia, allergies, hyperactivity, dermatitis, weight loss, decreased visual acuity, hair loss, delayed sexual development in boys, and chronic alcoholism.

The increased content of silicon in the hair can indicate a moderate violation of water-salt metabolism, with a tendency to urolithiasis, osteochondrosis, arthrosis, kidney, hair, nail, bronchial and lung diseases. Cobalt is integral part of vitamin B12, the lack of which is most noticeable in the hematopoietic tissues of the bone marrow and nerve tissues, and can also lead to degenerative changes in the spinal cord, Addison-Birmer anemia and developmental delay in children.

Iodine is necessary for normal functioning of the thyroid gland. Thyroid gland secretes hormones thyroxin and triiodothyronine, which are necessary for the synthesis of iodine. Especially the hormones of the thyroid gland depend on the processes of growth, development and general tone. The lack of hormonal iodine affects children and adolescents. Iodine has a calming effect on the body and the nervous system. There is a need for iodine to relax the body and its optimistic mood at nervous tension, irritability, insomnia. At normal providing in body iodine there is increasing mental activity.

Thus, the stable level of the "metallome" is a critical factor in cellular homeostasis, and individual element graph is a dynamic indicator of the MLH and could serve both for preclinical diagnosis and subsequent planning of personalized treatment and prevention.

In summary, we can conclude that a personalized approach to each patient using genomic, metabolomic, metallomics and possibly other technologies increases the effectiveness of treatment has specific therapeutic effects, reduces the risk of unwanted side effects, eliminates error assignment ineffective drugs reduces the cost of treatment and develops a preventive trend in medicine.

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