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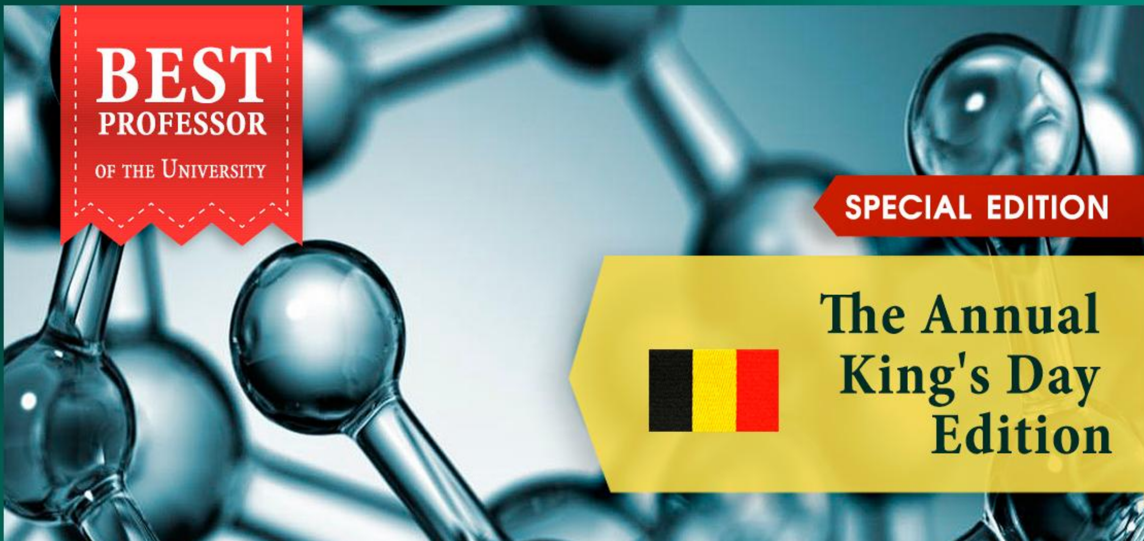

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THE ROLE OF OMIKS TECHNOLOGY IN THE FORMATION OF THE CONCEPT OF PERSONALIZED MEDICINE AND SOME RESULTS OF A STUDY OF «METALLOM»

Kamalidin O. Sharipov[1] (Skamalidin@mail.ru), **Galya M. Sayakova**[1] (avicenna.kz@bk.ru) **Raushan Dosymbekova**[1] (dos.raushan@mail.ru), **Konstantin A. Bulygin**[1] (kostyaapr@mail.ru)
Aigul A. Batyrbayeva[2] (batyrbaeva_aigul@mail.ru), **Perizat A. Mekessova**[2] (mekessova@mail.ru)
Danagul Y. Narmaganbetova[2] (Daneka94@mail.ru)

1 – Asfendiyarov Kazakh national Medical University, 2 – Al-Farabi Kazakh national Univercity
Almaty, Kazakhstan

Abstract

This paper examines the role of omiks technologies in the formation of the concept of personalized medicine, as well as some preliminary results of a study of «metallome». This shows a stable level components of the «metallome» is a critical factor in cellular homeostasis, and individual element graph is a dynamic indicator metalloligands homeostasis – MLH and can serve both for preclinical diagnosis and subsequent planning of personalized treatment and prevention.

Keywords: omiks technology, personalized medicine, metabolome, «metallome», genome, metabonom, individual element graph

RELEVANCE

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

The emergence of personalized medicine, the basic principle of which is the selection of treatments according to the genetic characteristics of patients and their diseased cells, stimulated the increasing flood of genetic data and diagnostic approaches, which began with the deciphering of the human genome. Before the subject of attention in medicine was the concept of personalization, individual approach was used, for example, in blood transfusion, transplantation of tissues, cell therapy and in the selection of drugs and dietary Supplements for correction of metabolic violations. Individualization of treatment is implied in genomic medicine as asymptomatic identification of predisposition to a particular disease, preventive measures, pharmacotherapy, and individual selection of treatment regimens performed on the basis of the genotype determination. Genotyping is an important basis, but in the development of personalized medicine there are other omiks technologies, such as the study of the metabolome, metabonome, «metallome» etc.

Metabolomes is the «systematic study of the unique chemical «fingerprints» of specific processes occurring in living cells» — more specifically, the study of their molecular and metabolic profiles [1]. Metabolome represents the collection of all metabolites that are the end product of metabolism in the cell, tissue, organ or organism [7] which can be found in a biological sample and in a single organism [4,12]. In January 2007 scientists at the University of Alberta and University of Calgary finished the first version of the human metabolome. They catalogued approximately 2500 metabolites, 1200 drugs and 3500 food components that can be found in the human body [14]. This information is available in the database of the metabolome person (www.hmdb.ca) and based on the analysis of existing scientific literature, is far from complete. Other organisms are much more well-known in regards to metabolomes. For example, there were over 50,000 metabolites of plants characterized, many thousands have been identified and characterized in isolated plants [2, 5].

Metabonome is defined as «quantitative measurement of dynamic multiparametric metabolic response of living systems to pathophysiological stimuli or genetic modification». The term comes from the Greek meta, meaning «change», and NOMOS, meaning «a set of rules or patterns» [9]. This approach was first proposed and used by Jeremy Nicholson at the Royal London College and is used in toxicology, disease diagnosis and a number of other areas. Historically metabolic approach was one of the first attempts to apply methods of systems biology to study metabolism [6, 10, 11].

Metallomics is a quantitative measurement of the components of the «metallome» products of the interaction of the ionic and atomic forms of metals with endogenous ligands (nucleotides, nucleosides, proteins, peptides, amino acids, carbohydrates and others). Recently the concept of metallomics increasingly include the study of not only metals in the body, but also of many vital micronutrients [3, 13].

Currently, the role of many macro– and micronutrients in the processes of growth, differentiation, regeneration, apoptosis and necrosis of cells and in the pathogenesis of several diseases, accompanied by significant changes in the elemental status of the body [13]. The imbalance me indirectly can be a triggering mechanism for the deregulation of apoptosis. Aggravating influence on the manifestation of a genotoxic effect of some metals has both the deficiency and excess or imbalance of some essential trace elements.

The results of years of research has shown that in a number of pathological processes observed unidirectional changes of the ratios of strictly defined elements, but different in absolute value [8]. Such a change in the element status is designated by Kaletin with co-authors as the primary (or preliminary) stress element graph. Against the background of continuing stress element graph in patients with clinically diagnosed there were additional changes of the element status specific to the disease and which are named by the authors mentioned above «specific element graph. According to the results, specific element graph may be an additional noninvasive diagnostic and prognostic test. The change in the absolute value of stress and specific element graph due to many factors, including genetic, environmental, diet, regimen.

The purpose of the present study was the determination of components of «metallome» i.e. macro-, trace elements in hair of residents of Kazakhstan and to develop a personalized approach to each patient based on the identified regularities of their changes in the body.

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). The object of investigations was the hair of the residents of Almaty aged 18-22 years. 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 to assess 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)).

RESEARCH RESULTS

The results of the instrumental study of the content of chemical elements in hair (element graph) were mostly in the normal range, and not a substantial deviation was different, as was to be expected. It should be noted that the content of calcium, phosphorus and potassium was above normal 10% of chromium, and sodium by 12% in the studied populations (Fig. 1). There were more specific abnormalities of essential trace elements such as cobalt, zinc and copper to the downside and silicon in the upward direction. The cobalt content was below reference intervals of variation of almost 1/3 part of surveyed groups of people.

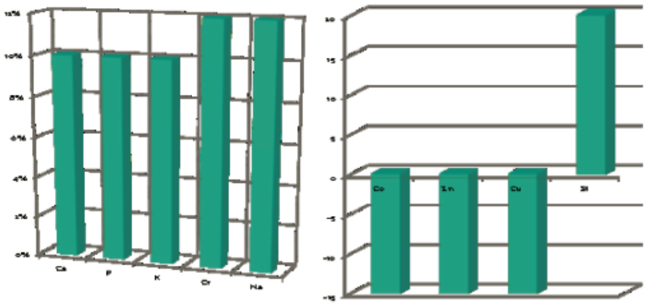

Figure 1. **Deviations from the reference intervals of some macro-, microelements**

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 to the largely long-lasting impact and nutritional factors. On a slight change of content in the hair calcium, phosphorus, potassium and sodium, we did not pay special attention, as this may be associated with age, lifestyle, social status, power and is usually short-lived. Multidirectional changes in the content of essential elements zinc, copper, chromium and especially a significant reduction in the level of cobalt may lead to certain orphan diseases or alarming requiring comprehensive research and personalized approach.

For example, in the human body copper affects the activity of more than 30 enzymes, stimulates cellular respiration, the production of female hormones and thyroxin. Copper ions facilitate the process of transfer of excitation in the brain. During fetal shortage of copper can cause heart disease. There are a number of genetic diseases in which the metabolism of copper leads to damage of brain, liver, musculoskeletal system, hair, Central nervous system disease (Konovalov-Wilson's, Menkes ' disease, multiple sclerosis). Copper metabolism is closely associated with zinc metabolism. Zinc activates about 200 different enzymes. Zinc deficiency is characterized by such symptoms as loss of appetite, anemia, allergies, hyperactivity, dermatitis, lack of weight, decrease of visual acuity, hair loss, delayed sexual development in boys, as well as chronic alcoholism.

The increased silicon content in the hair may indicate a moderate violation of water-salt metabolism, with a tendency to kidney stones, osteochondrosis, arthrosis, diseases of the kidneys, hair, nails, bronchi and lungs. Cobalt is a part of vitamin B12, lack of which is most noticeable in the hematopoietic tissues of the bone marrow and nerve tissues and can also cause degenerative changes in the spinal cord, Addison-Birmer anemia, and delayed development in children.

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. All this ultimately improves population health, quality of life and promote active longevity.

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