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Opinion

Preposition Genes Are Predictors of the Development of Multifactorial Diseases

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One of the most pressing problems in medicine is multifactorial diseases, i.e., diseases that have many causes in their genesis and as a result from the joint action of unfavorable environmental conditions and a number of genetic factors. This group of diseases includes arterial hypertension, ischemic heart disease, atherosclerosis, rheumatoid arthritis, schizophrenia, peptic ulcer, bronchial asthma, psoriasis, atherosclerosis, etc. Due to the complexity of the etiology and pathogenesis of such diseases, their study and diagnosis is much more difficult than monogenic [1,2,3,4].

At the same time, knowledge of the genetic foundations of multifactorial disease makes it possible to form the most rational recommendations for a particular patient on diet, lifestyle, physical activity, treatment, considering his individual characteristics. In addition, with the help of genetic tests, it is possible to obtain information about the long-term hereditary program of each person, which distinguishes them from biochemical, serological, and other analyzes that reflect the state of the body only at the moment. In this regard, the study of single nucleotide polymorphisms (SNP) and the creation on its basis of an individual genetic passport of a person become relevant [2,3].

The creation of a genetic passport made it possible to decipher the human genome and the development of methods of molecular genetics, which radically changed many aspects of clinical practice. Thanks to the international program "Human Genome", the main task of which was the letter-by-letter reading of all genetic information recorded in the human genomic DNA and the possibility of targeting the biochemical route prescribed in the genes, clinicians received an effective tool for treating patients, prolonging life, and improving its quality.

Genetic certification, or genotyping, is of enormous importance for medicine. Building individual genetic maps, collecting and analyzing a set of data on polymorphisms in a certain population group, determining the medical significance of mutations, mapping diseases by groups - is one of the most urgent tasks not only of human genetics, but also of practical medicine [2].

Comparative analysis of the differences between the genomic profiles of groups of patients and control groups of healthy people makes it possible to identify genes responsible for the development of a specific pathology. Currently, data have been published on several thousand polymorphisms that affect the change in biochemical processes in the human body. Knowledge of the genetic foundations of the pathological process makes it possible to determine the genetic characteristics of the disease of an individual patient (gene diagnosis), based on which recommendations are drawn up for a full range of preventive measures [2,3].

At the same time, the "genetisation" of medicine has led to the emergence of a new promising direction - predictive medicine. It, in contrast to medical and even preventive medicine, is appropriate to consider as the first and earliest stage of a person's active influence on his body in order to timely correct a potentially possible pathology or pathological process.

By combining the roles of all participants in genetic influence (genes) into one consolidated picture, it is possible to determine

with a high degree of certainty the medical prognosis of the tested organism - to predict what awaits a person, both in the near and in the distant future. Accordingly, this will be the solution to the problem posed by predictive medicine [1,2,3].

Genes, allelic variants of which, in the presence of certain conditions, predispose to certain diseases, and called "predisposition" genes. It is known that genetic polymorphism (a variety of genes limited to one species) inherent in humans leads to certain variations in the structure of proteins and, thereby, forms the biochemical individuality of each individual [2].

Polymorphism includes such variants of genes that arose because of point mutations a long time ago and spread in the population, going beyond the boundaries of individual families. Many variant genes are associated with a significant increase in the risk of developing a number of diseases [3,4]. The advantage of genetic diagnostics is that it makes it possible to identify a tendency to a particular disease long before its clinical manifestations, to take preventive measures in time, preventing its development or facilitating its course, and, taking into account individual characteristics, apply therapy.

One example of the association of genetic changes with disease phenotype found before the era of genome-wide genotyping is the ApoE variants and late-onset Alzheimer's disease. In this unusual case, a frequent haplotype of nonsynonymous codon variants in the ApoE gene was found to be strongly linked to Alzheimer's disease. It has been repeatedly shown that the risk allele (Apo4, defined by R112 and R158 in a homozygous state, 15 times increases the risk of Alzheimer's disease compared to other combinations of alleles [5]. After the introduction of genome-wide genotyping, several reports have described a close association of the complement control factor H gene with the course of age-related macular degeneration - AMD (ARMD) [6].

Many works have shown the role of genetic changes in the pathogenesis of such multifactorial diseases of the cardiovascular system as atherosclerosis, ischemic heart disease, arterial hypertension, heart failure. Genetic factors of predisposition to the development of diseases are more reliable than pathophysiological ones, since they can be detected before the appearance of pathological changes. In recent decades, many gene polymorphisms have been identified that claim to be genetic markers of cardiovascular diseases [7,8].

So, one of the socially significant diseases is atherosclerosis, which underlies the occurrence and development of ischemic diseases of the heart and brain. The disease has a complex etiology that includes a number of genetic and environmental factors. Genetic factors include polymorphic variants of genes responsible for lipid metabolism, inflammatory reactions, adhesion, and vascular remodeling factors [9,10].

A number of studies have shown that mutations T3336C, G13513A, G14459A of mitochondrial genes of subunits 1, 5, and 6 of NADH-ubiquinone oxidoreductase are associated with atherosclerotic lesions. The C5178A mutation, localized in the gene of subunit 2 of NADH-ubiquinone oxidoreductase, predominates in the normal intima, which indicates its antiatherogenic effect [10]. Mutation in the signal sequence of SOD2 (mitochondrial isoenzyme) Ala16Val in humans is a minor marker of carotid atherosclerosis [11,12,13].

The "weak link" genes are associated with the duration of the active longevity period: mitochondrial DNA, ApoE4, ApoA1, MTHFR, ACE, PON, GSTM1, CYP17A1, IL10, TNFA. It should be noted that the genes of the weak link are very numerous and belong to different metabolic systems of the body [3,4].

Currently, in developed countries, methods of pharmacogenetics are increasingly used - the direction of medical genetics and pharmacology, which studies the genetic characteristics of patients that affect the pharmacological response. The main interest is currently focused on the field of pharmacogenetics, which analyzes changes in genes involved in the metabolism of drugs, with special emphasis on enhancing their safety, since metagenomic studies conducted in the USA and Europe have demonstrated that adverse drug reactions drugs cause about 106 thousand deaths and 2.2 million.

The patterns revealed by pharmacogenetics allow the doctor to individually approach the choice of both the drugs themselves and their dose for each individual patient, providing the most effective and safe pharmacotherapy [14].

Thus, timely identification of risk factors for development with subsequent pathogenetically justified therapy and appropriate preventive measures can reduce the risk of multifactorial diseases.

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Conflict of Interest

No conflict of interest.

References

1. Aimoldina, GR Batpenova, G Zh Abildinova, TV Kotlyarova, TV Tarkina, et al. (2014) Vitiligo genetics: the role of hereditary A factors in the onset of vitiligo. Astana medicine journal 3(81): 10-18.
2. AA Nagimtayeva, AV Borovikova, BO Kamaliyeva, GZh Abildinova (2014) Genetic certification and genodiagnostics - a new direction in predictive medicine. Astana medicine journal 3(81): 37-43.
3. Francis S Collins and Leslie Fink (1995) The Human Genome Project. Alcohol health & research world 19(3): 190-195.
4. Z Ahmed, S Zeeshan, D Mendhe, XinQi Dong (2020) Human gene and disease associations for clinical-genomics and precision medicine research. Clinical and Translational Medicine 10(1): 297-318.
5. EE Blue, A Cheng, S Chen (2020) Association of Uncommon, Noncoding Variants in the APOE Region with Risk of Alzheimer Disease in Adults of European Ancestry. JAMA Network Open | Neurology 3(10): e2017666.

6. MR Speicher, SE Antonarakis, AG Motulski (2013) Human genetics according to Vogel and Motulski. Problems and approaches. SPb.: Publishing house NL 5(1): 73-74.

7. VN Kovalenko, EB Kuchmenko, LS Mhitaryan (2014) The role of single nucleotide polymorphisms and mirnas in the pathogenesis of diseases of the cardiovascular system. Journal of the National Academy of Medical Sciences of Ukraine 20(1): 62-73.

8. Naghshtabrizi B, Shakerian F, Hajilooi M, Emami F (2018) Plasma homocysteine level and its genotypes as a risk factor for coronary artery disease in patients undergoing coronary angiography. J. Cardiovasc. Dis. Res 4(4): 276-283.

9. Alexandra M Dainis, Euan A. Ashley, DPhila (2018) Cardiovascular Precision Medicine in the Genomics. JACC Basic Transl Sci 3(2):313-326.

10. Era Perrino C, Barabási AL, Condorelli G, Sean Michael Davidson, Leon De Windt, et al. (2017) Epigenomic and transcriptomic approaches in the post-genomic era: path to novel targets for diagnosis and therapy of the ischaemic heart? Position Paper of the European Society of Cardiology Working Group on Cellular Biology of the Heart. Cardiovasc Res. V 113(7): 725-736.

11. A Volobueva, A Grechko, SF Yet, I Sobenin, A Orekhov (2019) Changes in Mitochondrial Genome Associated with Predisposition to Atherosclerosis and Related Disease. Biomolecules 9(8): 377.

12. Crawford A, Fassett R G, Gereghty DP, Dale A Kunde, Madeleine J Ball, et al. (2012) Relationships between single nucleotide polymorphisms of antioxidant enzymes and disease. Gene 501: 89-103.

13. Bilgin E, Can Demirdöğen B, Türkanoğlu Özçelik A (2018) Association analysis of Glutathione S-transferase omega-1 and omega-2 genetic polymorphisms and ischemic stroke risk in a Turkish population. Neurol Res 10: 1-7.

14. Akbari H, Asadikaram G, Vakili S, Masoumi M (2018) Atorvastatin and losartan may upregulate renalase activity in hypertension but not coronary artery diseases: The role of gene polymorphism. Journal of Cellular Biochemistry 120(6): 9159-9171.