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Opinion

Genetic Resistance to Infectious Diseases in the Era of Personalized Medicine

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Individual particularities of resistance to pathogens have been the focus of clinicians and researchers for centuries. Several theories and concepts were formulated to explain this phenomenon. They include the immunological theory of infectious diseases, the genetic theory of infectious diseases, the concept of latent and asymptomatic infection, monogenic and polygenic type of inheritance of resistance to pathogens and a number of others [1]. Nowadays, most of these concepts are reflected in the modern theory called "A Unified Genetic theory of infection disease". The theory assumes that at an early age susceptibility to pathogenic microorganisms is caused by inherited variants of genes, while in adults features of a disease course depend on the total action of several genetic loci. In elderly people, a special role in the initiation and development of infectious disease plays somatic mutations [2]. In this regard, recently developed methodological approaches to wide genome analysis allow us to hope for a significant expansion of our understanding of genetic resistance to infectious diseases at both individual and population levels.

In recent decades, significant progress has been made in the study of genetic resistance to the pathogens of the genus Mycobacterium: M. tuberculosis (causes tuberculosis), M. leprosy (causes leprosy), and M. ulcerans (causes Buruli ulcer). The collected data clearly demonstrate the polygenic nature of resistance to these diseases, which is important for creating a strategy for monitoring resistance/susceptibility to these infections within the framework of personalized medicine concept [3].

Another large series of studies is linked to immunity to P. Falciparum, which causes malaria. It was shown that some loss of function mutations provide resistance. Such mutations are displayed in genes: α-globin, ß-globin, Glucose-6-phosphate dehydrogenase, Duffy antigen/chemokine receptor, ABO transferase, HLA-B. According to modern estimates, most genes have mutated centuries ago. Mutations were common in several populations [4].

Resistance to viral diseases is also actively studied. A number of intracellular mechanisms ensuring resistance to viral infections have been identified [5]. Mutations which provide immunity to human immunodeficiency virus [6], parvovirus B19 [7], norovirus [8] are well known.

Research on model animals is of great importance for understanding the genetic mechanisms of predisposition to infectious diseases. The genetic law of homologous series suggests that mutations and molecular mechanisms found on animal models may exist in humans too. Recently, a new mechanism of resistance to pathogens of the genus Salmonella has been identified on the model of Mus musculu. The mechanism is based on the interaction between the subtypes of T- and B-lymphocytes [9]. Genetic resistance of Sus domesticus to enterotoxigenic F18+ E. coli infections is also well-known. The allelic variant of the FUT1 gene encoding fucosyltransferase provide the resistance [10]. In recent years significant progress has been made in the study of resistance to transmissible spongiform encephalopathies of Capra hircus [11]. The alleles of resistance to avian leukemia virus was mapped for Gallus gallus domesticus [12]. New achievements in this area are steadily growing.

Thus, it is no doubt that an important direction of modern genetics of infectious diseases is the search for allelic variants of genes that provide resistance/ susceptibility to pathogens. These studies should combine both advances in human molecular genetics and comparative analysis of resistance to pathogens of other species. Only joint efforts of all specialists in this field: clinicians, microbiologists, geneticists and bioinformatics will make it possible to create individual maps of resistance/predisposition to pathogens for humans. The creation of such maps is a part of the personalized medicine of the future.

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