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# Influence of FABP2 Gene Polymorphisms in Athletes Involved in Cyclic Sports

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**Abstract:** Sports genetics is still at the beginning of the path, but at the same time it opens up many prospects for the development of biomedical support for sports. Using the genetic characteristics of the body will lead mankind to new records, because now not only perseverance, regular training, willpower and motivation of an athlete are important, but also his "Olympic" heredity. The use of modern molecular genetic methods allows us to identify individual characteristics of the human body. A detailed study of these genes is necessary for the proper organization of the training process, for predicting the capabilities of athletes. According to modern concepts of functional genomics, it is believed that individual differences in the degree of development of certain physical and mental qualities, as well as susceptibility to certain diseases of athletes are largely due to DNA polymorphisms (variable regions in the DNA sequence).

**Keywords:** sports medicine, sports genetics, prediction of athletes' capabilities, selection of athletes, DNA polymorphisms.

The success of athletes in high-level competitions is an important component of the country's international prestige. In this regard, the situation regarding the importance of the health of athletes for their achievement of high sports results has become particularly relevant [4; 7; 9]. The results of scientific research have shown that the basis of the optimal indicators of the health of athletes is the state of dynamic balance between the functional reserves of the body and the factors affecting it [1; 2; 3]. At the same time, the magnitude of the influence of factors that are inherent in the modern system of training athletes on the body of those involved increases in proportion to the stages of their professional development, which requires not just optimal health indicators, but the presence of an appropriate level of reserves for the functions of its components [7; 12; ]. The value of the latter is the basis of the athlete's reliability - an indicator that is characterized by high performance and its stability in extreme conditions of activity [5]. In this regard, there is a consensus among specialists that athletes-children and adolescents have the lowest reliability coefficient, since it is this contingent of those involved in sports that has certain prerequisites for the development of disadaptation disorders in somatic systems, the structural elements of which are included in the newly formed system of body adaptation to muscle activity. [13; 16;]. These prerequisites include specific features of the structure of the child's body, biochemical processes and functions in general, as well as individual organs in which qualitative (development) and quantitative (growth) changes occur at various stages of ontogenesis [2; 3; 8]. In addition, the failure of regulatory systems and the heterochrony of the processes of growth and maturation only aggravate the problem of the development and progression of pathological abnormalities in the somatic systems of the body of young athletes with an irrational construction of the training process, which is confirmed by

scientific research data on the incidence of child athletes [3; 11; 12]. Despite the ongoing preventive and therapeutic measures, the number of somatic diseases in reserve athletes does not statistically decrease [13; 14; 16], which allows us to state the presence of a number of issues, the solution of which is associated with the development of the concept of physical rehabilitation of young athletes with dysfunctional disorders of somatic systems mediated by training and competitive activities.

Currently, predictive medicine is actively developing, the purpose of which is to identify possible diseases in a particular patient by the DNA structure, as well as to develop a set of preventive or recreational measures based on these studies. Such preventive measures are also important in sports, so sports genetics allows you to achieve high results using scientific methods.

A lot of data, including the results of recent studies, confirm the influence of certain gene polymorphisms on the physical characteristics of an athlete and, as a result, on the predisposition of the athlete's body to power loads or endurance training.

It must be taken into account that the development and manifestation of the physical qualities of a person depends on both genetic and environmental factors. The more genetic factors affect physical qualities (high degree of heritability), the less successfully these qualities are trained, and vice versa [1].

Sports genetics allows you to calculate the limit of each person to perform any type of exercise, depending not only on the nature of the task, but also on genetic components. The human genotype largely determines such important characteristics for athletes as strength, endurance, muscle fiber composition and muscle mass, flexibility, neuromuscular coordination, and reaction speed [2].

Over the past few decades, certain hereditary factors responsible for the development of the above qualities in humans have been established. Therefore, sports genetics provides useful information on how to improve performance, which athletes to select for competitions and which of them will be able to cope with the task. The selection of young, promising in terms of their hereditary qualities of athletes (at the same time minimal risk of intense physical activity for their health) is an important issue in sports medicine, which can be solved by modern methods of genetics. The introduction and active use of molecular genetic technologies makes it possible to create an optimal training program specifically for each athlete, in which the energy resources of the body will be used as efficiently as possible, which will allow achieving high sports results. I would also like to note that due to the active development of genetics as a science and methods of its study, genetic research is becoming more and more accessible. At the moment, sports genetics is present not only in elite sports, but also in amateur sports. Fitness is an important component of a healthy lifestyle, and its proper organization should be approached responsibly. In this case, based on a genetic study, a geneticist can recommend a specific diet, diet, training regimen, as well as the nature of the exercises, taking into account the individual characteristics of the body. In addition, sports genetics makes it possible to identify diseases to which a person is genetically predisposed (for example, cardiovascular diseases, bronchial asthma, obesity). Based on the data obtained, it is possible to recommend preventive measures to prevent these diseases for each individual.

Sports genetics is a young science, at the moment it is only 38 years old. It was proclaimed as a branch of knowledge at the Olympic Scientific Congress "Sport in Modern Society", which was held in Tbilisi in 1980. Also, the "International Scientific Society for Sports Genetics and Somatology" was created there. In 1983, Claude Bouchard first proposed the term "genetics of physical (motor) activity" (genetics of fitness and physical performance). Then he published two reviews in one issue of the journal "Exercise and Sport Science reviews", where he presented generalizing facts, firstly, about individual differences in response to physical activity, and secondly, about the heritability of many qualities involved in the process of physical activity [3] . 1995 was marked by the beginning of the international project HERITAGE (HEalth, RIsk Factors, Exercise Training And Genetics) under the leadership of Claude Bouchard. The project involved several research centers and more than 800 volunteers who were exposed to physical activity for several weeks. K. Bouchard and his colleagues searched for polymorphic loci associated with physical activity and published hundreds of papers on the heritability of human physical factors. Progress in understanding this issue has been significant.

In 1998, the scientific article "Human gene for physical performance" by a young British scientist Hugh Montgomery was published in the journal Nature. He presented the results of his work with a team of authors (19 people) to study the role of the ACE (angiotensin converting enzyme) gene in sports activities. H. Montgomery and his colleagues studied a group of alpine climbers [4]. The size of the article is only one page, which says that one of the polymorphic alleles of the ACE gene - the I allele provides endurance, and the D allele - speed-strength qualities of an athlete. The conclusion was based on the fact that athletes who are successful in endurance sports have a higher frequency of the I allele than in the control group, while the D allele predominates in athletes of speed-strength sports [5, 6]. This publication attracted the attention of the entire scientific community and society as a whole. The world media reported on the discovery of a "sport gene" (ACE gene), thanks to which it was now possible to identify a predisposition to a certain sport or physical activity in any person.

Sports genetics is developing quite rapidly, as the number of new studied genes that characterize the physical qualities of a person is growing exponentially: in 1997 - 5 genes; in 2000 - 24 genes; In 2004, 101 genes [8]. To date, about 200 genetic markers (DNA polymorphisms) are known to be associated with the development and manifestation of physical qualities [9]. In sports, in order to achieve the highest performance, talented athletes must be selected correctly and in a timely manner, and then included in long-term, planned training programs [10]. Today, due to the fact that investments in sports and individual athletes reach serious amounts, the issue of effective selection of athletes is more relevant than ever [10]. Each of us is individual, we carry unique genetic information. And our uniqueness can be studied using DNA diagnostic methods, which show the features of metabolism, the state of organ systems, and the properties of the psyche. In sports genetics, for a detailed study of genetic material, such molecular genetic methods as PCR, real-time PCR, RFLP analysis, QTL mapping, NGS, NNGS, biochip technology, as well as cytogenetic methods (karyotyping, fluorescence in situ hybridization or the method FISH), genealogical and biochemical research methods. It is inexpedient and irrational to perform DNA typing for all possible genes responsible for human athletic characteristics. The information received must be correctly interpreted and conclusions drawn in relation to each individual case. At the same time, the analysis of one gene is not informative enough. Genetic analysis provides information about the genetic predisposition to a particular sport. For example, skeletal muscles are made up of two separate types of muscle fibers: fast and slow. Slow fibers are characterized by a small force of contraction, but low fatigue, they are involved in the performance of low-intensity strength work for a long time. Fast fibers, on the contrary, are characterized by greater force of contraction and high fatigue; they are involved in the performance of short, high-intensity strength work [11]. For muscles that are dominated by slow fibers, aerobic exercise will be the most effective. Such sports are swimming, rowing, tennis, long-distance running, cycling, and walking. And for muscles, which are dominated by fast muscle fibers, anaerobic exercise (strength training) is most effective. Wrestling, sprinting, powerlifting, arm wrestling, rock climbing are examples of motor activity based on anaerobic muscle metabolism. The type of muscle fibers that prevail in our body is genetically determined (this is associated with the polymorphism of the ACE gene). So, the results of a stayer (long-distance runner) in the 2000-meter run are negatively correlated with his results in the 100-meter run. When the type of exercise matches the genetic predisposition, a person can achieve better results and get the maximum effect from training in the shortest possible time.

Fatty acid binding protein (FABP2) is widely distributed in epithelial cells of the small intestine and has been identified as one of the genes that regulate intracellular metabolism. FABP2 is responsible for the absorption and intracellular transport of dietary long chain fatty acids (LCFA) [95]. The SNP results from the conversion of guanine at codon 54 of the FABP2 gene to adenine, an alanine-coding allele and a threonine-coding allele (Ala54Thr). Agren, J et al. showed that carriers of the Thr54 allele have a 2 times higher affinity for LCFA than carriers homozygous for the Ala54 allele. In vitro allele substitutions that increase the affinity of FABP2 for LCFA (such as Ala54-Thr54) are associated with increased triglyceride transport in human intestinal cells. In addition, Thr54 substitution has been shown to be associated with insulin resistance, increased fatty acid binding, and increased fat oxidation. Baier et al. reported that among a population of non-diabetic Pima Indians, Ala54 homozygotes (40M/28F), heterozygotes (28M/29F), and Thr54 homozygotes (7M/5F)

homozygous or heterozygous for the threon-encoding allele were found to have a higher mean fasting plasma insulin concentration ($p<0.04$), lower mean insulin-stimulated glucose uptake rate ($p<0.04$), higher mean insulin response to oral glucose and mixed meals, and higher mean oxidation state fat ($p < 0.002$) compared to Pimas, which were homozygous for the allan-coding allele. However, according to these data; Martinez-López [100] showed that during an 8-week very low calorie diet (VLCD) intervention, Thr54 allele carriers experienced more favorable responses to a moderate fat diet among Hispanic ($n = 109$) overweight participants. These conflicting results may indicate that genotype does not necessarily differentiate changes in weight loss, fitness, or biochemical health measures when introduced into a dietary intervention such as caloric restriction. Table 2.2 presents weight loss intervention studies for the FABP2 SNP.

Recent studies have demonstrated the high effectiveness of diet and physical activity in correcting metabolic disorders. With lifestyle changes in people with early disorders of carbohydrate metabolism, the risk of developing type 2 diabetes mellitus (T2DM) is reduced by 58%. However, it is also known that in some patients, diet and increased physical activity are ineffective and do not prevent the development of the disease. Today, a new approach to building a diet based on the individual characteristics of a person is proposed. The influence of nutritional components on gene expression is being studied by a new science - nutrigenomics. Nutrients can cause changes in metabolism by affecting the activity of certain genes, which in turn affect the human proteome and metabolome. In addition, the genetic variability of foods themselves can have an impact on human health. Nutrients can influence the genome of the microbial flora of the gut, which also causes changes in metabolism. Thus, the subject of nutrigenomics is the study of interactions between food genomes, the human genome, and the genomes of the gut microbiota. Changes in gene activity that occur during the growth and development of an organism are called epigenetic. Epigenetics is the study of changes in gene expression that occur without altering the nucleotide sequence of deoxyribonucleic acid (DNA). There are three mechanisms of epigenetic changes: DNA methylation, histone modification, and RNA interference (suppression of gene expression by small molecules of ribonucleic acid). It is assumed that the components of the diet can affect the processes of DNA methylation [1]. First, nutrients are important in providing and regulating the synthesis of S-adenosylmethionine, the universal methyl group donor. Secondly, they can affect the utilization of methyl groups through changes in the activity of DNA methyltransferase. The third possible mechanism is related to the activation of DNA demethylation [2]. Currently, a large number of genes have been identified, the polymorphism of which is associated with the development of metabolic disorders. It turned out that food components can change the activity of these genes. Published results of studies that demonstrate the existence of an interaction between a number of genes associated with obesity and type 2 diabetes, and some foods. Examples of such interactions are presented below as examples. Fatty acid binding protein type 2 (FABP2) is an intracellular protein produced in enterocytes. It is involved in the transport and metabolism of long chain fatty acids, and can also maintain cellular homeostasis by acting as a lipid sensor. The FABP2 gene is located on chromosome 4q28-q31.

The polymorphism of this gene is associated with an increased risk of developing type 2 diabetes. This is because the protein it encodes is involved in fatty acid absorption and therefore can affect insulin sensitivity and glucose metabolism. There are three genotypes: normal or so-called wild type (Ala54/Ala54), heterozygous (Ala54/Thr54) and homozygous (Thr54/Thr54). Heterozygous and especially homozygous Thr54 genotype is associated with the development of insulin resistance, type 2 diabetes, and possibly increased cardiovascular risks. A meta-analysis of 31 studies that examined 13,451 people showed that the FABP2 gene mutation, namely the presence of the Thr54 allele, is associated with more pronounced insulin resistance, elevated fasting plasma insulin levels, and increased glycemia levels 2 hours after glucose loading [3]. It has been found that FABP2 expression may depend on adherence to a certain diet. D. de Luis et al. studied the dynamics of body weight and a number of metabolic markers in response to a hypocaloric diet (1459 kcal/day) rich in polyunsaturated fats (22.7% of the total fat consumed per day) in obese individuals with FABP2 gene polymorphism (Thr54) . The decrease in body mass index, body weight, and waist circumference was significantly more pronounced in the group with the Thr54 allele compared to

individuals with the wild type of the FABP2 gene allele. Moreover, only in carriers of the Thr54 allele, while following a diet enriched with polyunsaturated fats, a significant decrease in total cholesterol, low-density lipoprotein cholesterol, and insulin was noted [4]. In another study, it was shown that individuals with obesity and FABP2 gene polymorphisms (Ala54/Thr54 and Thr54/Thr54) who followed a hypocaloric diet (1342 kcal) with a high content of monounsaturated fats (67.5%) did not have a significant change in biochemical markers, despite the improvement in anthropometric indicators. On the contrary, in the carriers of the wild allele for this gene, while following the proposed diet, in addition to weight loss, the levels of insulin, leptin, and insulin resistance significantly decreased [5]. Thus, based on nutrigenomic studies, it should be concluded that people with FABP2 gene polymorphisms (Ala54/Thr54 and Thr54/Thr54) are shown a diet high in polyunsaturated fatty acids (about 20% of the total fat consumed per day). To do this, it is enough to introduce fatty fish into the diet (about 750 g per week) or take fish oil regularly.

**Findings.** A genetic approach to the problem of sports orientation, selection of athletes will undoubtedly help to avoid "marriage" in coaching, save from performing ineffective work and ensure high rates of training of athletes. With the help of genetic analyzes, it is possible to determine not only a predisposition to a particular sport, but also to identify possible health problems that can become a serious obstacle to sports victories. Based on the recently obtained results on the decoding of the human genome, research is currently being carried out all over the world using molecular genetic methods to identify the degree of heritability of morphological and functional features of a person. The latest data obtained in the course of these molecular genetic studies, contributing to the individualization and optimization of the training process, create the possibility of achieving high sports results, which is confirmed by the setting of new records by athletes in various prestigious competitions.

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