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Role of Peroxisome Proliferator Activated Receptor Alpha (*PPARA*) rs4253778 Polymorphism in Endurance Phenotype

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Introduction

An individual's athletic performance is determined with the intersection of the genetic endowment that he/she owns, and its interaction with environmental factors such as training, nutrition, mentoring and sleeping[1]. Around 70% of the variance in athletic performance is explained by genetic factors. Environmental factors play crucial roles in effecting the expression of several genes; and all of these subjects are examined under the topic of epigenetics. As of today, a total of 250 genes are considered to have effect on human performance, and the number seems to increase as we have the new molecular high-through put techniques that are introduced to molecular genetics, it is now possible to analyse hundreds of SNPs in only on application.

The need for identifying genetic variants contributing to athletic performance has been challenging because of the possible involving of the examined genes that are considered to have a minor phenotypic effect. But when we consider the total effect of these genetic variant, a huge contribution is apparent, and to have information on these variants, we will have a chance to speculate on the cumulative effect of these variants on athletic performance[2].

One of the important markers of these variants is peroxisome proliferator activated receptor alpha (*PPARA*) intron 7G/C polymorphism (rs4253778). The *PPARA* is located on chromosome 22 (22q12-q13.1). PPARs are members of the nuclear hormone receptor super family and *PPARA* codes for transcriptional factor named nuclear receptor protein peroxisome proliferator activated receptor alpha (PPAR-alpha)[3]. *PPARA* gene has been a good candidate gene to study athletic ability because its protein product has important roles in lipid metabolism, vascular inflammation and glucose energy homeostasis[4]. Recent studies showed the expression levels of the gene can be regulated with environmental factors, for example in some conditions of energy deprivation and during metabolic and physiological stress, such as in fasting[5] and hypothetically also during endurance sports[6]. And also there is evidence that this gene is involved in the immune responses of the human body to endurance training, as it enables activation of the fatty acid oxidation mitochondrial pathway[7].

One of the important SNPs in the gene is rs4253778. The HaploReg database predicted this SNP as a variation that alter in binding sites for members of the IRF family of transcription factors (encoded by 9 genes in humans: IRF1-IRF9)[8]. This polymorphism is located in intron 7, the non-coding region of the gene, and therefore it can be considered to be non-functional. However, like other SNPs located in introns and have important phenotypic effects, there is a possibility that this polymorphism is in linkage disequilibrium with a functional variant in any region of the PPAR-alpha gene that can result in PPAR-alpha gene expression[6]. In addition, there is evidence that this gene interacts with other variations in the peroxisome proliferator - activated receptors[9,10,11] and with other genes such as the apoA-I and apoB genes[12]. Therefore, it is important that further studies are needed to fulfill these interactions and effects in endurance sports.

G allele of rs4253778 is linked with increased fatty acid

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oxidation and an increased proportion of type I slow twitch fibres in skeletal muscles, these fibres use oxygen in a more efficient manner during continuous muscle activity. Endurance athletes have relatively more type I slow twitch than fast twitch fibres in the trained musculature, which permits a sustained muscular contraction over a long period of time[13]. Furthermore, the GG genotype of rs4253778 was shown to be correlated with high values of oxygen pulse[14]. Therefore this genotype became one of the important genetic marker for aerobic activities, like endurance phenotype[15]. On the other hand, C allele of the PPARα gene is thought to be associated with higher plasma lipid levels cardiac growth, and increased risk of coronary artery disease[16].

Some studies demonstrated that the frequency of the *PPARA* rs4253778 GG genotypeand G allele was statistically higher in elite Polish rowers[17], Polish combat athletes[18], Russian endurance-oriented athletes[15] and elite Israeli endurance athletes[19], compared with controls and/or sprinters.

Determining genetic endowment and regulating personal training strategies is important for success in sports. Not only the mentioned variation, all related polymorphisms, alone- or in combination with the additional polymorphisms, should be taken into account when deciding a genomics core profile for success in sports.

Conflict of Interest: All of the authors have no conflict of interest to declare.

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