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Genome-Wide Association Study Reveals a Novel Association Between MYBPC3 Gene Polymorphism, Endurance Athlete Status, Aerobic Capacity and Steroid Metabolism

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Abstract

 Background: The genetic predisposition to elite athletic performance has been a controversial subject due to the underpowered studies and the small effect size of identified genetic variants. The aims of this study were to investigate the association of common single-nucleotide polymorphisms (SNPs) with endurance athlete status in a large cohort of elite European athletes using GWAS approach, followed by replication studies in Russian and Japanese elite athletes and functional validation using metabolomics analysis. Results: The association of 476,728 SNPs of Illumina DrugCore Gene chip and endurance athlete status was investigated in 796 European international-level athletes (645 males, 151 females) by comparing allelic frequencies between athletes specialized in sports with high (n = 662) and low/moderate (n = 134) aerobic component. Replication of results was performed by comparing the frequencies of the most significant SNPs between 242 and 168 elite Russian high and low/moderate aerobic athletes, respectively, and between 60 elite Japanese endurance athletes and 406 controls. A meta-analysis has identified rs1052373 (GG homozygotes) in Myosin Binding Protein (MYBPC3; implicated in cardiac hypertrophic myopathy) gene to be associated with endurance athlete status (P = 1.43 × 10−8, odd ratio 2.2). Homozygotes carriers of rs1052373 G allele in Russian athletes had significantly greater VO2max than carriers of the AA + AG (P = 0.005). Subsequent metabolomics analysis revealed several amino acids and lipids associated with rs1052373 G allele (1.82 × 10–05) including the testosterone precursor androstenediol (3beta,17beta) disulfate. Conclusions: This is the first report of genome-wide significant SNP and related metabolites associated with elite athlete status. Further investigations of the functional relevance of the identified SNPs and metabolites in relation to enhanced athletic performance are warranted.

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Keywords

elite athletes, endurance, GWAS, metabolites, metabolomics, SNP

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