



The association of *HFE* gene H63D polymorphism with endurance athlete status and aerobic capacity: novel findings and a meta-analysis

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Abstract

Purpose Iron is an important component of the oxygen-binding proteins and may be critical to optimal athletic performance. Previous studies have suggested that the G allele of C/G rare variant (rs1799945), which causes H63D amino acid replacement, in the *HFE* is associated with elevated iron indexes and may give some advantage in endurance-oriented sports. The aim of the present study was to investigate the association between the *HFE* H63D polymorphism and elite endurance athlete status in Japanese and Russian populations, aerobic capacity and to perform a meta-analysis using current findings and three previous studies.

Methods The study involved 315 international-level endurance athletes (255 Russian and 60 Japanese) and 809 healthy controls (405 Russian and 404 Japanese). Genotyping was performed using micro-array analysis or by PCR. VO_{2max} in 46 male Russian endurance athletes was determined using gas analysis system.

Results The frequency of the iron-increasing CG/GG genotypes was significantly higher in Russian (38.0 vs 24.9%; OR 1.85, $P=0.0003$) and Japanese (13.3 vs 5.0%; OR 2.95, $P=0.011$) endurance athletes compared to ethnically matched controls. The meta-analysis using five cohorts (two French, Japanese, Spanish, and Russian; 586 athletes and 1416 controls) showed significant prevalence of the CG/GG genotypes in endurance athletes compared to controls (OR 1.96, 95% CI 1.58–2.45; $P=1.7 \times 10^{-9}$). Furthermore, the *HFE* G allele was associated with high VO_{2max} in male athletes [CC: 61.8 (6.1), CG/GG: 66.3 (7.8) ml/min/kg; $P=0.036$].

Conclusions We have shown that the *HFE* H63D polymorphism is strongly associated with elite endurance athlete status, regardless ethnicities and aerobic capacity in Russian athletes.

Keywords Gene · Genotype · Hemochromatosis · Endurance performance · Athletes

Abbreviations

CI Confidence intervals
DNA Deoxyribonucleic acid
EDTA Ethylenediaminetetraacetic acid
GWAS Genome-wide association studies
HFE Homeostatic iron regulator (hemochromatosis gene)

HH Hereditary hemochromatosis
HWE Hardy–Weinberg equilibrium
PCR Polymerase chain reaction
RFLP Restriction fragment length polymorphism
SNP Single-nucleotide polymorphism
STREGA Strengthening the reporting of genetic association
TFRC Transferrin receptor
 VO_{2max} Maximal oxygen consumption

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