Exercise and sport genetics

Genes and Sports Differences in the physical fitness and athletic capabilities in humans are affected by the interaction of environmental (e. g. diet and training) and genetic factors. Studies from the last thirty years show that genetic variations strongly influence cardiorespiratory and skeletal muscle function, and thus, performance of athletes (MacArthur & North, 2005). Modern molecular techniques for rapid genotyping and DNA sequencing made it possible to identify genetic variations in the traits that contribute to athletic performance.

Studies on twin pairs and nuclear families provided the earliest data to on the heritability of variations in fitness-related traits (Bouchard, Leon, Rao, Skinner, Wilmore, & Gagnon, 1995). In these studies, 130 two-generation families were monitored for different responses to an aerobic exercise program implemented for twenty weeks. Oxygen uptake, stroke volume, cardiac output, and exercise heart rate response to training were found to be heritable. Genetics was also found to influence other variables such as skeletal muscle strength and performance, muscle adaptation to endurance exercise, explosive power, muscle strength, and their response to training. Segregation analysis showed that mostly single genes are responsible for phenotypic variation in some traits like oxygen uptake at the ventilator threshold (Feitosa, et al., 2002). These findings have resulted in the identification of polymorphisms and genetic loci that contribute to human physical performance.

Genome-wide linkage analyses and genetic associations identified cardiorespiratory and skeletal muscle performance genes. Studies using the HERITAGE family cohort (Bouchard et al. 1995) identified linkage peaks associated with genetic variation in maximal oxygen uptake, power output,

exercise stroke volume, blood pressure, body fat distribution, glucose and insulin metabolism (MacArthur & North, 2005). Association studies have further identified three candidate genes involved with cardiorespiratory function. The first was CKMM, which encodes for the cytosolic muscle isoform of creatine kinase, is responsible for the rapid regeneration of ATP during intensive muscle contraction. This gene was associated with exercise performance (Rivera, et al., 1997). Second was the angiotensinogen gene, AGT, M235T missense polymorphism, which has positive association with several measures of cardiorespiratory performance (McCole, et al., 2002). Missense polymorphisms in the ADRB2 gene for the β2-adrenergic receptor were also found to be associated with cardiorespiratory performance traits (Moore, Shuldiner, Zmuda, Ferrell, McCole, & Hagberg, 2001). Other polymorphisms were also identified to have potential correlation with athletic performance.

Case-control studies in elite athletes have identified the angiotensin-converting enzyme (ACE) insertion/deletion polymorphism (I/D) as a genetic factor with a very strong influence on physical performance (Montgomery, et al., 1998). ACE is important in the circulatory system; it degrades vasodilator kinins, and converts angiotensin I (ATI) to the vasoconstrictor angiotensin II (ATII). The ACE gene has two alleles, insertion, or I allele and deletion or D allele, which differ in the presence (I) or absence (D) of a 287-bp Alu repeat element in intron 16. The I variant is associated with lower ACE levels and better endurance in a study of mountaineers (Montgomery, et al., 1998) and British Olympic-standard runners (Myerson, Hemingway, Budget, Martin, Humphries, & Montgomery, 1999). It was also observed that there was an increased frequency of the D allele in 35 elite short-distance swimmers

(Woods D, et al., 2001), suggesting that the ACE I/D polymorphism have differing effects on athletic performance. Endurance is associated with the I allele and power events are with the D allele.

Interestingly, there was no association between the ACE gene variants and the endurance of Kenyan athletes (Scott, et al., 2005). It was noted that despite many positive association studies, larger studies do not find any evidence for the association, especially when the grouping became more heterogeneous (MacArthur & North, 2005). Nevertheless, despite the difficulties in validating the association between performance and ACE in large cohorts, the ACE genotype is proposed to improve maximal oxygen uptake, muscle endurance and muscle contraction.

Another gene associated with elite athlete status is a null polymorphism (R577X) in the ACTN3 gene encoding α-actinin-3, which is part of the sarcomeric apparatus of fast-fibres of the human skeletal muscle (MacArthur & North, 2007). Genotype frequency determinations showed that the absence of α-actinin-3 was beneficial for male endurance runners but not in female athletes. This absence lowers the performance of sprint athletes, considering that the polymorphism removes the expression of the fast-fibre protein in skeletal muscle.

The identification of genes that are related to physical performance can be utilized in sports for the selection of athletes and the formulation of training regimes. Nevertheless, it is still necessary to validate and integrate all the conflicting data from studies already conducted.

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