

## Overcoming the barrier of sample size: The ACTN3 R577X polymorphism across three groups of elite European athletes

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The ACTN3 R577X common polymorphism was identified by North *et al.* (1999). We (Eynon *et al.*, 2009), and the Norths group (Yang *et al.*, 2003), have previously observed a significantly lower frequency of ACTN3 577XX ( $\alpha$ -actinin-3 null), in elite power athletes (*i.e.* sprinters, jumpers and throwers) compared to healthy controls. In contrast, elite endurance athletes (*i.e.* long-distance runners and triathletes) had higher frequencies of the ACTN3 577XX genotype compared to controls (Eynon *et al.*, 2009; Yang *et al.*, 2003). Subsequently, this association has been replicated in several cohorts of elite athletes from different ancestries, with some studies unable to find a significant association with performance possibly due to sample size limitation (Eynon *et al.*, 2011). In fact, most of the aforementioned studies performed with elite athletes were limited by a relatively low sample size ( $n \leq 200$ ). In the present study, for the first time, we were able to recruit over 600 elite male athletes from three different European countries in an attempt to overcome this barrier.

**Aim:** To compare the frequency distribution of the ACTN3 R577X polymorphism between elite endurance athletes, elite sprint/power athletes, and ethnically-matched, non-athletic controls in a large group of European Caucasians, from Spain, Poland and Russia. We also examined the association of the ACTN3 R577X with respect to the performance level (world-class and national level) of both endurance and power athletes.

**Methods:** A total of 633 athletes (endurance athletes  $n=278$ ; sprint/power athletes  $n=355$ ) and 808 controls, from Spain, Poland and Russia, were genotyped for the ACTN3 R577X polymorphism. All participants were unrelated European males and all Caucasians for  $\geq 3$  generations. We included athletes in the study sample only if they had participated in national/international championships.

**Results:** The odds ratio (OR) of having the XX genotype *vs* having the RR genotype (co-dominant effect) for male power athletes was 0.54 (95% confidence interval (CI): 0.34-0.48;  $P=0.006$ ) compared with sedentary controls. The OR of having the XX genotype *vs* having the RR (co-dominant effect) for endurance athletes was 1.88 (95% CI: 1.07-3.31;  $P=0.006$ ) compared with power athletes. The OR of having the XX genotype *vs* having the recessive trait for endurance world-class athletes was 3.74 (95% CI: 1.08-12.94;  $P=0.038$ ) compared with endurance national-level athletes.

**Conclusion:** Our data provide strong support for the potential influential role of the ACTN3 R577X polymorphism to elite athletic status.

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