Association of MMP3 but not TIMP2 gene variants with elite rugby player status and rugby code

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Introduction

Achilles tendon pathology and anterior cruciate ligament rupture are multifactorial conditions for which genetic risk factors have been identified1-3. Single nucleotide polymorphisms (SNPs) within the MMP3 (rs591058, rs679620, rs650108) and TIMP2 (rs4789932) genes have previously been associated with tendon and ligament pathologies4,5,6,7. Although not entirely clear, prior literature indicates the risk alleles for Achilles tendon pathology as T (rs591058), G (rs679620) and A (rs650108) for MMP3. However, prior evidence regarding TIMP2 is equivocal8. MMP3 is considered an essential regulator of matrix degradation and remodelling within diseased and normal musculoskeletal soft tissues8. TIMP2 maintains homeostasis in the extracellular matrix in part by inhibiting MMP function. Given the high incidence and severity of tendon and ligament injuries in elite rugby athletes, we hypothesised that the aforementioned SNPs would be associated with career success.

Method

Participants were from the RugbyGene project, comprising elite Caucasian male rugby athletes (n = 528; mean (standard deviation) height 1.85 (0.07) m, mass 101 (14) kg, age 29 (7) yr), including 420 rugby union (RU) athletes that for some analyses were divided into forwards and backs and 108 rugby league (RL) athletes. Non-athletes were 592 Caucasian men and women (57% male, height 1.72 (0.10) m, mass 74 (14) kg, age 31 (7) yr). PCR of genomic DNA was used to determine genotypes using TaqMan probes, then groups were compared using χ² and odds ratio (OR) statistics.

Results

As hypothesized, the MMP3 rs591058 risk genotype (TT) was less frequent in rugby athletes (28%) compared to non-athletes (33%) (Figure 1) (χ² = 7.265, P = 0.002; OR = 1.18, 95% confidence intervals (CI) = 0.86-1.63). No differences were found for MMP3 rs679620, rs650108 or TIMP2 rs4789932 between rugby athletes and non-athletes. When RL athletes were compared to non-athletes, the risk genotype (TT) of MMP3 rs591058 was underrepresented in RL athletes (19%) compared to non-athletes (33%). The MMP3 rs679620 ‘protective’ allele (C) was more frequent in RL athletes (55%) compared to non-athletes (48%) (OR = 1.3, 95% CI = 0.98-1.74) (Figure 2). However, for MMP3 rs650108 the ‘risk’ allele (A) was overrepresented in RL athletes (32%) compared to non-athletes (26%). There were no genotype differences for any gene variant between RU athletes and non-athletes. The ‘risk’ allele (T) of the MMP3 rs679629 polymorphism and the ‘protective’ allele (G) of the MMP3 rs650108 polymorphism were less common in RL (45%, 68%, respectively) than RU athletes (54%, 76%, respectively)(Figure 3).

Conclusion

We provide evidence for elite rugby athletes possessing a protective genetic profile regarding tendon and ligament injury risk. Notably, a less frequent MMP3 TT genotype in athletes suggests a lower risk of injury could therefore enhance career success in rugby. Furthermore, RL players appear to have differing genetic characteristics compared to their RU counterparts, which might reflect some differences in physiological demands between codes.

References


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