

ACTN3 R577X genotype is associated with bone formation markers in humans

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Background: Osteocalcin (OC) is a marker of bone formation, while the undercarboxylated form of OC (ucOC) modulates insulin sensitivity. Exercise increases serum ucOC levels, however, there is large variation between individuals. This variation is potentially influenced by the presence (RR and RX genotypes) or absence (XX genotype) of α -actinin-3 protein (*ACTN3* R577X common variant), as the protein is expressed in osteoblasts, bone cells that secrete OC and ucOC.

Aim: To examine whether the *ACTN3* R577X influences changes in OC and ucOC pre-and-post exercise.

Methods: Forty-four healthy Caucasian individuals (Age: 30.1 \pm 1.4 years, BMI=25.5 \pm 0.4 kg·m⁻²) were divided into three groups (*ACTN3*XX, N=13; *ACTN3*RX, N=16; *ACTN3*RR, N=15). Participants completed a single session of High Intensity Interval Exercise (HIIE) on a cycle ergometer (8 \times 2-min intervals at 85% of maximal power with 1 min of recovery between intervals). Blood samples were taken before, immediately after, and three hours post exercise to identify the peak change in OC and ucOC.

Results: At baseline, XX individuals had a higher OC level compared to their RR counterparts (37.3 \pm 3.9 vs 28.2 \pm 1.7 ng/mL, $P=0.04$). ucOC was similar across genotypes (all $p > 0.37$). Following HIIE, OC levels increased only in RX individuals (~9%, $P=0.001$), whereas ucOC level increased in all three groups (XX ~8%, $P=0.02$; RX ~11%, $P=0.006$ and RR ~7%, $P=0.08$).

Conclusion: Individuals with *ACTN3* XX variation are characterized by a higher circulating levels of OC, which may indicate a higher bone remodelling compared to RR individuals. The response of ucOC to exercise is not explained by *ACTN3* R577X.