

## Bone Health, ACE Gene I/D and ACTN3 Gene R577X Polymorphisms in Spanish And Different Asian Populations

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Osteoporosis is characterized by deterioration of skeletal micro-architecture, as well as low bone mineral density (BMD). Osteoporosis can lead to an increased risk of fragility fracture, meanwhile low BMD is recognized as a major risk factor for osteoporotic fracture. To date, a large number of studies used BMD as the major surrogate phenotype for osteoporotic fracture. Bone mineral density is a quantitative trait determined by genetic factors with an influence ranging from 50% to 90%; nevertheless, it is also known that a higher BMD is related to physically active lifestyles. In the field of exercise and sports science, the two popular genes, i.e., Angiotensin converting enzyme (ACE) gene and Alpha-actinin-3 (ACTN3) gene are regarded as main genetic factors which are related to human physical fitness, such as muscular performance, aerobic and anaerobic capacities in different populations all around the world [1-4].

The human ACE gene contains a restriction fragment length polymorphism consisting of the insertion, I (presence of Alu repeat) and deletion, D (absence of Alu repeat) of 287 bp of Alu repeat located in intron 16 (rs1799752). ACTN3 gene, which encodes the protein  $\alpha$ -actinin-3, contain a polymorphism which replaces arginine (R) to stop codon Ter (X) (rs1815739) at position 577 of amino acid and results in the deficiency of  $\alpha$ -actinin-3 protein. To our knowledge, to date a few studies have been performed to evaluate whether ACE I/D and ACTN3 R577X polymorphisms are associated with bone health and osteoporosis [5-11].

Regarding studies in older populations, a study on Caucasian Spanish by Pérez-Castrillón et al. [6] found that hypertensive postmenopausal women with ACE gene II genotype had a higher BMD than those with ID and DD genotypes in this study. Lynn et al. [7] carried out a study to evaluate the affection of ACE gene I/D polymorphism on osteoporosis treatment with Asian population involving 1,958 Chinese males and 1,929 females. It was found that a better therapeutic effect was observed in participants with ACE gene II genotype compared to those with ID or DD genotype. In Turkish population, Cakmak et al [5] reported that a higher frequency of ACE DD genotype and D allele was observed in 238 osteoporosis female patients compared to 124 healthy controls (DD genotype). Bayram et al. [8] also observed that DD genotype was related to osteoarthritis in a Caucasian Turkish population. Nevertheless, Hong et al. [9] reported that there was no association between ACE I/D polymorphism and osteoarthritis in the Asian Korean population.

In a recent study by Kim et al. [10], 856 Korean preadolescent children were recruited to examine the association between ACE I/D and ACTN3 R577X polymorphisms and early bone age. It was found that lower early bone age was observed in children with the combination of ACE II, ACE ID and ACTN3 XX genotypes compared to those with other genotypes. These findings suggested that bone growth and metabolism i.e. early maturity might be effected by ACE DD genotype in Korean preadolescent children [8]. Meanwhile, Zebrick et al. [11] reported that participants with skeletal Class II malocclusion overrepresented a higher frequency of ACTN3 XX genotype compared to controls, and suggested that bone growth might be influenced by this genotype.

ACE is a component of circulating renin-angiotensin system (RAS) which influences circulatory homeostasis through the degradation of vasodilator kinins and generation of vasopressor angiotensin II (Ang II). It is a monomeric, membrane-bound, zinc- and chloride-dependent peptidyl dipeptidase that catalyzes the conversion of decapeptide angiotensin I to octapeptide angiotensin II, by removing carboxy terminal dipeptide. In our opinion, it is worth to investigate whether it exerts genetic influence on the interaction among muscular system, circulating RAS and bone components, based on the fact that ACE I/D and ACTN3 R577X are two most common physical fitness-related variations, and the precise roles of ACE I/D and ACTN3 R577X polymorphisms on bone mineralization are still unclear.

Different frequency of ACE I/D and ACTN3 R577X polymorphisms have been reported in different populations worldwide, and human body is a complicated combination and organization which is influenced by multiple factors, i.e., race, lifestyle, environment and nutrition, as well as genetic and training etc.. Therefore, a question arises: Is there single or multiple factors that can influence skeletal development in different populations? To answer this question, continuous effort is warranted to search for the associations between genetic markers such as ACE I/D and ACTN3 R577X polymorphisms, bone health and other factors in different populations.

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### Competing Interests

The authors declare no conflict of interest.

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