

**THE JOINT EFFECT AND INTERACTIONS BETWEEN TUMOR NECROSIS FACTOR GENE AND INTERLEUKIN-6 GENE ON BONE MINERAL DENSITY IN COMMUNITY-DWELLING ELDERLY IN TAIWAN-TAICHUNG COMMUNITY HEALTH STUDY FOR ELDERLY (TCHS-E)**

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**Purpose:** The present study explored the joint effect and interactions between tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) gene and interleukin-6 (IL-6) gene on bone mineral density (BMD), by investigating six single-nucleotide polymorphisms (SNPs) of two genes in community-dwelling elders in Taiwan.

**Methods:** Six SNPs (rs1799964 [S1], rs1800629 [S2], and rs3093662 [S3] in TNF- $\alpha$  gene; rs1880243 [S4], rs1800796 [S5], and rs1554606 [S6] in IL-6 gene) were utilized to genotype 472 unrelated elderly subjects (221 women and 251 men). Bone mineral density (BMD, g/cm<sup>2</sup>) of the lumbar spine (LS), the femoral neck (FN), and the total hip (TH) were measured by Dual-energy X-ray absorptiometry. The lowest value of BMD among LS, FN, and TH sites was defined as his/her overall BMD value.

**Results:** In the women and men, in combination in TNF- $\alpha$  SNPs S2 & S3, and TNF- $\alpha$  SNPs S2 as well as IL-6 SNPs S4, S6, S5, were stronger significant joint effects on BMD by adjusted age, BMI, smoking and physical activity. The risk of BMD is greatest in subjects with the TNF- $\alpha$  SNPs S2 minor allele A versus those with G allele. We obtained evidence of a statistical interaction between S2-S4 and S4-S5 at FN BMD, S2-S4 at TH BMD, S2-S4 at lumbar spine (LS) BMD in elderly women was significant ( $P < .05$ ).

**Conclusion:** These results provide evidence that statistical joint effect and gene-gene interactions can be detected on BMD in elders.

**Key words:** bone mineral density, gene, single-nucleotide polymorphisms, joint effect, interaction

**THE INFLUENCE OF BOTH TUMOR NECROSIS FACTOR A AND INSULIN-LIKE GROWTH FACTOR-1 POLYMORPHISMS ON LEAN MUSCLE MASS IN COMMUNITY-DWELLING ELDERLY IN TAIWAN-TAICHUNG COMMUNITY HEALTH STUDY FOR ELDERLY (TCHS-E)**

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**Purpose:** This study examined the influence of both tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) and insulin-like growth factor-1 (IGF-1) polymorphisms on lean muscle mass, by investigating six single-nucleotide polymorphisms (SNPs) of two genes in community-dwelling elders in Taiwan.

**Methods:** Six polymorphisms of TNF- $\alpha$  (SNPs rs1799964 [S1], rs1800629 [S2], and rs3093662 [S3]) and IGF-1 (SNPs rs6214 [S4], rs5742692 [S5], and rs35767 [S6]) genes were examined in 472 participants (221 women and 251 men). Site-specific lean muscle mass (arms, legs, and trunk; kg), appendicular skeletal muscle mass (ASM; kg), and total body lean soft tissue mass (free-fat mass, FFM; kg) were measured by Dual-energy X-ray absorptiometry. Height-adjusted skeletal muscle index (hSMI; kg/m<sup>2</sup>) was defined as ASM divided by height squared. Weight-adjusted skeletal muscle index (wSMI; %) was tallied as ASM divided by weight.

**Results:** The joint effects between TNF- $\alpha$  and IGF-1 polymorphisms included S1 & S5 and S1 & S6 with arm lean muscle mass in the women group, and included S3& S4, S3& S5 and S3 & S6 with 3 site-specific lean muscle mass (arms, legs, and trunk), FFM, ASM, hSMI and wSMI in the men group. In the women and men, in combination in TNF- $\alpha$  SNPs S1 & S2 and S1 & S3, were significant joint effects on lean muscle mass by adjusted age, BMI, smoking and physical activity. We received evidence of a statistical interaction between S4 and S6 at legs lean soft tissue mass in elderly women was significant ( $P < .05$ ).

**Conclusion:** Our data show that an observed joint effect and interaction between TNF- $\alpha$  and IGF-1 polymorphisms on lean muscle mass in elders.

**Key words:** lean muscle mass, gene, single-nucleotide polymorphisms, joint effect