# Genomics of Bone: Single Nucleotide Polymorphism in Ostoporosis

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Osteoporosis is a multifactorial disease characterized by reduced bone mass, deterioration of bone microarchitecture, increased bone fragility and increased risk of fracture. Genetic factors are known to account for 46-85% of bone mass. Therefore, it is useful to identify genetic markers that are associated with low bone mass for prediction of risk of osteoporosis and prevention of the disease. The Skeletal Genome Research Cencer (SDGRC) (http://bone.knu.ac.kr) is devoting to collect national genome resources, to identify, and to analyze SNPs related to osteoporosis and arthritis, and to understand a role of genes involved in bone diseases. It also includes development of DB for genomic variations in Korean society, diagnostic DNA chip and animal models related to osteoporosis and arthritis.

Recently, we studied the possible association of bone mass and the risk of fracture with genes associated with osteoporosis: osteoclast associated receptor (*OSCAR*), receptor activator of NF-kB (RANK, also called tumor necrosis factor receptor superfamily 11A (*TNFRSF11A*)), Catalase (*CAT*), MTHFR/MTRR, Plexin A2 (*PLXNA2*), and Semaphorin 7a (*SEMA7A*). These genes play critical roles during osteoclast or osteoblast differentiation as well as function. Through direct sequencing of 24 Korean individuals, we identified sequence variants in each gene and genotyped in postmenopausal Korean Woman (n=560). *OSCAR2322A>G* promoter polymorphism showed significant and susceptible effects on BMD at various bone sites and the risk of vertebral fracture in postmenopausal women. These findings suggest that the *OSCAR* gene is a candidate for genetic determinants of BMD and fracture risk in postmenopausal women. Also we found *RANK+34863G>A* and *RANK+35928insdelC* showed an association with BMD at the lumbar spine, total femur, Ward's triangle and trochanter, but not the risk of vertebrate fracture. These findings suggest that polymorphisms in *TNFRSF11A* are associated with BMD in the limited regions of bone. In addition, *CAT+22348C>T* and *CAT ht4* were associated with high BMD of lumbar spine (L2-L4). They were also associated with low concentration of blood osteocalcin. Through the continual efforts to identify multiple SNPs associated with low BMD or the risk of osteoporosis, we are going to establish the Korean Bone SNP DB. In this way, the Korean Bone SNP DB may be greatly useful for single gene association study, for gene-gene interaction study, and hopefully for gene to environment interaction study.