

OSTEOSCOOP

News on current events in osteoporosis and rheumatology

Multiple genetic loci for bone mineral density and fractures

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Bone mineral density influences the risk of osteoporosis later in life and is useful in the evaluation of the risk of fracture. A recent study from Iceland [1] aimed to identify sequence variants associated with bone mineral density and fracture. A quantitative trait analysis of data was performed from 5861 Icelandic subjects (the discovery set), testing for an association between 301 019 single-nucleotide polymorphisms (SNPs) and bone mineral density of the hip and lumbar spine. The authors then tested for an association between 74 SNPs (most of which were implicated in the discovery set) at 32 loci in replication sets of Icelandic, Danish, and Australian subjects (4165, 2269, and 1491 subjects, respectively).

Sequence variants in five genomic regions were significantly associated with bone mineral density in the discovery set and were confirmed in the replication sets. Three regions are close to or within genes previously shown to be important to the biologic characteristics of bone: the receptor activator of nuclear factor- κ B ligand gene (RANKL) (chromosomal location, 13q14), the osteoprotegerin gene (OPG) (8q24), and the estrogen receptor 1 gene (ESR1) (6q25). The other two regions are close to the zinc finger and BTB domain containing 40 gene (ZBTB40) (1p36) and the major histocompatibility complex region (6p21). The 1p36, 8q24, and 6p21 loci were also associated with osteoporotic fractures, as were loci at 18q21, close to the receptor activator of the nuclear factor- κ B gene (RANK), and loci at 2p16 and 11p11.

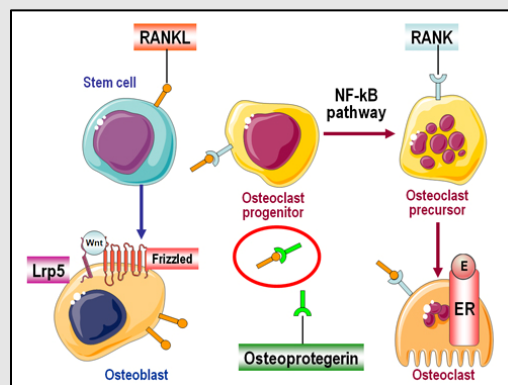
This study reports therefore the discovery of common sequence variants that are consistently associated with bone mineral density and with low-trauma fractures in three populations of European descent. Although these variants alone are not clinically useful in the prediction of risk to the individual person, they provide insight into the biochemical pathways underlying osteoporosis.

1. Styrkarsdottir U et al. N Engl J Med. 2008;358:2355-2365.

Multiple genetic loci for bone mineral density and fractures

Polymorphisms of osteoprotegerin and Lrp5 were recently reported to be associated with low bone mineral density, osteoporosis and fractures. As reported in a recent study, polymorphisms of RANK, RANK ligand, and the estrogen receptor were also associated with low bone mineral density and fractures.

Other polymorphisms of genes or regions which are not obviously related to bone physiology were discovered, raising the possibility that modifier genes are involved in bone remodelling.



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