A genomic and transcriptomic approach to the high bone mass phenotype: evidences of heterogeneity and of additive effects of TWIST1, IL6R, DLX3 and PPARG

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RESULTS

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Prevalence of HBM in the BARCOS cohort = 0.6%

OBJECTIVES

- To establish the prevalence of the high bone mass phenotype in the BARCOS cohort of postmenopausal Spanish women
- To determine whether any of the HMB cases carry LRP5 or DKK1 mutations that explain the phenotype
- To test the hypothesis of an inverse correlation between the number of common variant osteoporosis risk alleles and HBM
- To characterize the expression pattern of osteoblast-specific and Wnt pathway genes in primary osteoblast RNA samples from two HBM cases

INTRODUCTION

High bone mass (HBM) was defined as an asymptomatic autosomal dominant condition characterized by increased bone mineral density (BMD) due to gain-of-function mutations in the LRP5 gene. In the general population, BMD is normally distributed, and at the high extreme of the curve people display BMD values similar to those found in HBM patients (Fig. 1).

The range of densities of HBM is defined by:

\[(\text{LS Z score} + \text{Hip Z score}) > 4\]

FIGURE 1. Distribution of BMD in healthy women aged 30-40 years. Values similar to HBM patients are highlighted in red. (Adapted from Kanaa 2002)

CONCLUSION

- LRP5 does not seem to be the cause of the HBM phenotype in these cases from BARCOS cohort.
- The BMD risk allele analysis showed an inverse correlation with BMD in the HBM group.
- The results of the expression study raise new hypotheses that should be further investigated.

The authors declare no conflict of interest