Common variants in the JAZF1 gene associated with height identified by linkage and genome-wide association analysis.

Genes for height have gained interest for decades, but only recently have candidate genes started to be identified. We have performed linkage analysis and genome-wide association for height in approximately 4000 individuals from five European populations. A total of five chromosomal regions showed suggestive linkage and in one of these regions, two SNPs (rs849140 and rs1635852) were associated with height (nominal P = 7.0 x 10(-8) and P = 9.6 x 10(-7), respectively). In total, five SNPs across the genome showed an association with height that reached the threshold of genome-wide significance (nominal P< 1.6 x 10(-7)). The association with height was replicated for two SNPs (rs1635852 and rs849140) using three independent studies (n = 31 077, n=1268 and n = 5746) with overall meta P-values of 9.4 x 10(-10) and 5.3 x 10(-8). These SNPs are located in the JAZF1 gene, which has recently been associated with type II diabetes, prostate and endometrial cancer.
JAZF1 is a transcriptional repressor of NR2C2, which results in low IGF1 serum concentrations, perinatal and early postnatal hypoglycemia and growth retardation when knocked out in mice. Both the linkage and association analyses independently identified the JAZF1 region affecting human height. We have demonstrated, through replication in additional independent populations, the consistency of the effect of the JAZF1 SNPs on height. Since this gene also has a key function in the metabolism of growth, JAZF1 represents one of the strongest candidates influencing human height identified so far.