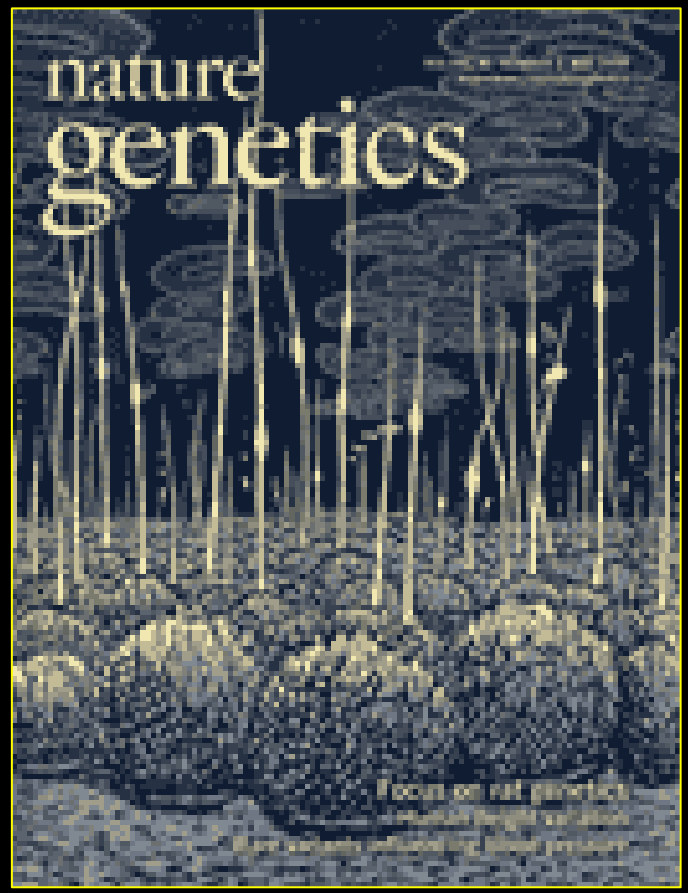

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Genome-wide association analysis identifies 20 loci that influence adult height

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Adult height is a model polygenic trait, but there has been limited success in identifying the genes underlying its normal variation. To identify genetic variants influencing adult human height, we used genome-wide association data from 13,665 individuals and genotyped 39 variants in an additional 16,482 samples. We identified 20 variants associated with adult height ($P < 5 \times 10^{-7}$, with 10 reaching $P < 1 \times 10^{-10}$). Combined, the 20 SNPs explain ~3% of height variation, with a ~5 cm difference between the 6.2% of people with 17 or fewer 'tall' alleles compared to the 5.5% with 27 or more 'tall' alleles. The loci we identified implicate genes in Hedgehog signaling (*IHH, HHIP, PTCH1*), extracellular matrix (*EFEMP1, ADAMTSL3, ACAN*) and cancer (*CDK6, HMGA2, DLEU7*) pathways, and provide new insights into human growth and developmental processes. Finally, our results provide insights into the genetic architecture of a classic quantitative trait.

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Identification of ten loci associated with height highlights new biological pathways in human growth

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Height is a classic polygenic trait, reflecting the combined influence of multiple as-yet-undiscovered genetic factors. We carried out a meta-analysis of genome-wide association study data of height from 15,821 individuals at 2.2 million SNPs, and followed up the strongest findings in >10,000 subjects. Ten newly identified and two previously reported loci were strongly associated with variation in height (*P* values from 4×10^{-7} to 8×10^{-22}). Together, these 12 loci account for ~2% of the population variation in height. Individuals with ≤8 height-increasing alleles and ≥16 height-increasing alleles differ in height by ~3.5 cm. The newly identified loci, along with several additional loci with strongly suggestive associations, encompass both strong biological candidates and unexpected genes, and highlight several pathways (*let-7* targets, chromatin remodeling proteins and Hedgehog signaling) as important regulators of human stature. These results expand the picture of the biological regulation of human height and of the genetic architecture of this classical complex trait.

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Many sequence variants affecting diversity of adult human height

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