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# International Collaboration and New Technology Reveal Rare Genes that Determine Height

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**INTRODUCTION:**
Height is a phenotype, an observable trait of the genes that we inherit from our parents. It's a polygenic trait, meaning it is controlled by 2 or more genes. Because it is so easy to measure, it is an ideal characteristic to help us understand other polygenic traits. So far, genome-wide association studies (GWAS) have identified 700 common variants that determine a person's height. New discoveries have been made by the international group called Genetic Investigation of Anthropometric Traits (GIANT), revealing 83 genetic mutations that have additional effects on a person's height[1]

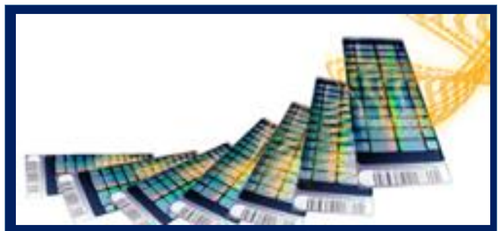

Figure 1: Illumina microarray Exomechip[3]

**METHODS:**
Researchers used new technology called the Exomechip; this is a human genotyping microarray that can process thousands of DNA samples to identify mutations and structural variants. Common variants have a minor allele frequency (MAF) of > 5%, and are located outside of DNA coding regions. The Exomechip can capture low frequency (MAF=1–5%) and rare (MAF < 0.5%) variants. Because of the identification of these mutations, geneticists can now account for 27% of the genetics determining height, which is an increase from 20% based on earlier studies.[1]

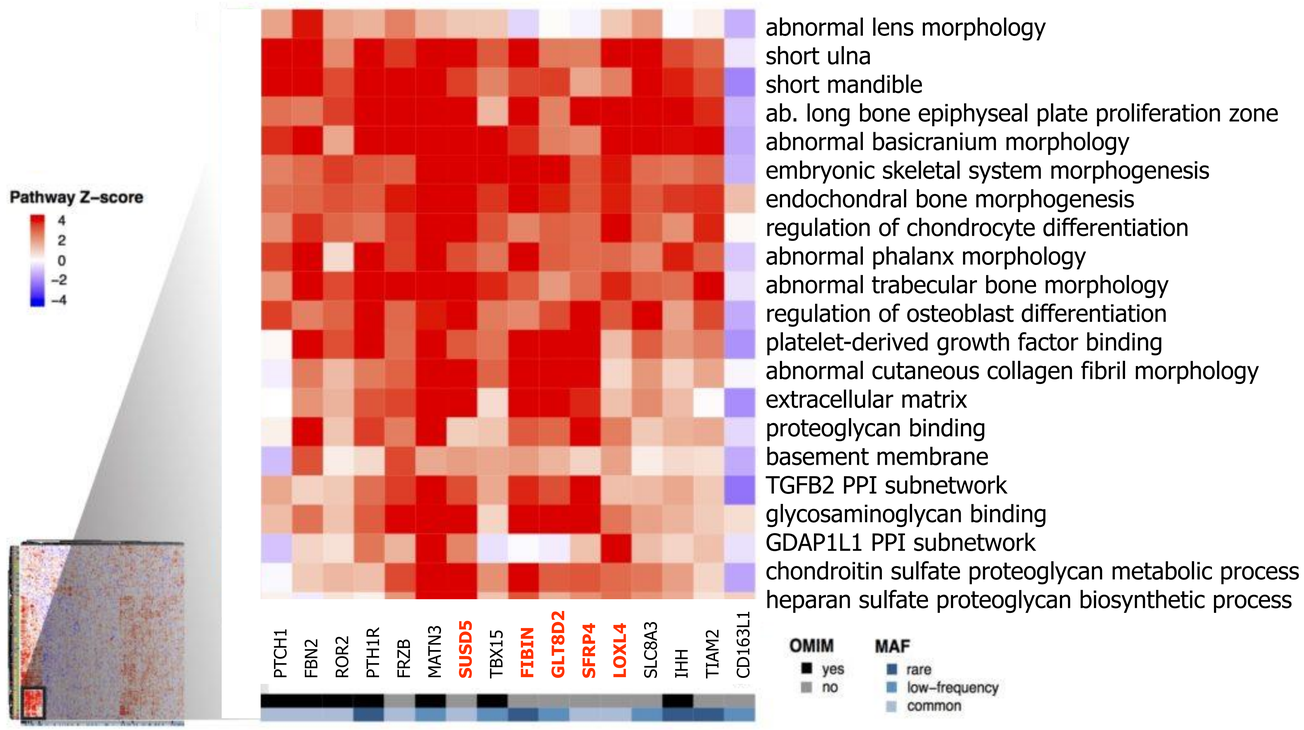


Figure 2: Height associated genes have shared biological connections. The redder squares indicate stronger connections between a gene and its predicted biological function. The genes that are highlighted had not previously been associated with skeletal growth. These gene variants can be used as a shortcut to figuring out which genes are important for a specific disease or trait.[2]

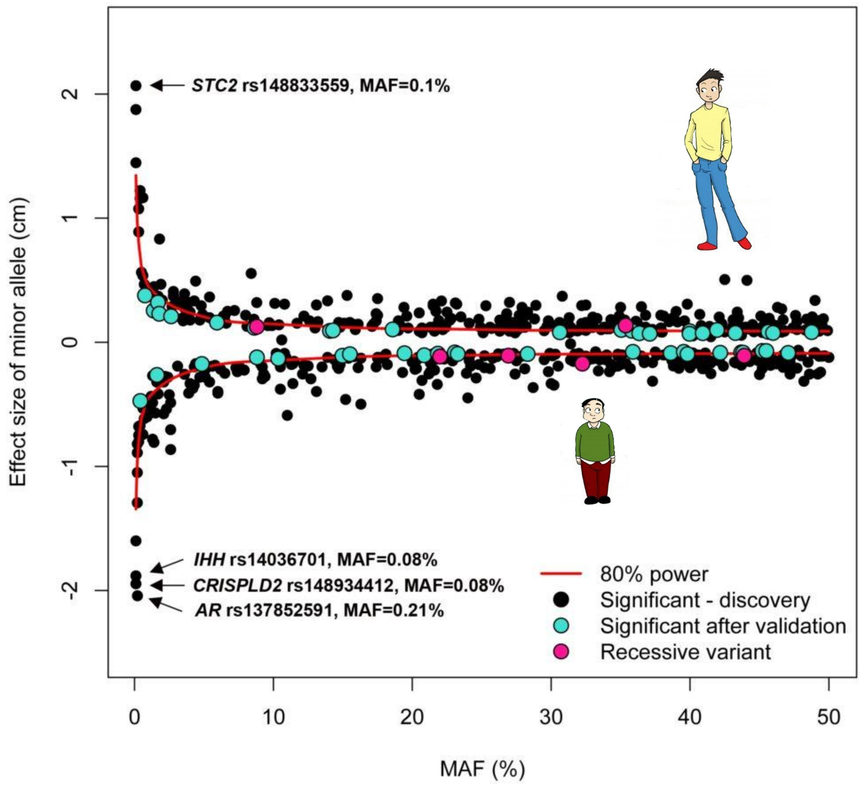


Figure 3: The STC2 gene had 2 different profoundly rare variants; one can be seen in the upper left corner. These very rare variants directly alter proteins, and have the strongest effects on increasing or decreasing height by affecting the availability of growth factors in the blood.[2]

- GIANT collaborated with Montreal Heart Institute, Queen Mary University, University of Exeter, UK and 280 other research groups
- This study involved over 700,000 adults: 460,000 initially and then 250,000 to validate the results.
- Researchers are already launching a GWAS of height that will include over 2 million people.[1]

Figure 4: Population image showing different ATGC nucleotide sequences[3]

**CONCLUSION:**
This gives us a better understanding of human growth and how these variations influence the structure of a complex polygenic trait. By identifying rare genetic mutations, scientists can investigate uncommon DNA changes involved in other aspects of human health, such as diabetes and heart disease, giving them a better understanding of those diseases and may then lead to better treatments.

**REFERENCES:**
(1) Marouli, Eirini, et al. "Rare and Low-Frequency Coding Variants Alter Human Adult Height." Nature, vol. 542, no. 7640, 09 Feb. 2017, pp. 186-190. EBSCOhost, doi:10.1038/nature21039.
(2) Boston Children's Hospital. "GIANT study finds rare, but influential, genetic changes related to height: International study of more than 750,000 people probes deeper into height than ever before." ScienceDaily, 1 February 2017. <www.sciencedaily.com/releases/2017/02/170201131513.htm>.
(3) https://www.illumina.com/techniques/popular-applications/genotyping/whole-genome-genotyping.html

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