



**INSTITUT DE
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**PRESS RELEASE
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We grow up for hundreds of little genetic reasons

A study led by researchers at the Montreal Heart Institute shows that hundreds of genetic variations determine the height of individuals

Montreal, September 29, 2010 – Hundreds of common genetic variations in the human genome influence people’s height, according to a major study published today in the journal *Nature*. For this new study, close to 300 researchers from 200 institutions within the GIANT Consortium (Genetic Investigation of ANthropometric Traits) analyzed the DNA of 183,000 individuals with the objective of identifying genetic variations called SNPs (single nucleotide polymorphisms, pronounced “snips”), which are associated with height.

Height is a complex genetic trait in that it is influenced by an individual’s genetic baggage and by his or her environment. In the specific case of height, an estimated 80% of the variation observed in a population is attributable to variations in DNA, with the remaining 20% attributed to environmental factors such as nutrition. “It is well known that height is determined mainly by heredity,” said Dr. Guillaume Lettre, co-director of the study and researcher at the Montreal Heart Institute, as well as associate professor at the Université de Montréal. “What we had yet to demonstrate prior to this publication was the sheer number of genes involved in growth and height.”

To identify genes that influence height, Dr. Lettre and his colleagues from the United States, the United Kingdom and the Netherlands used a pangenomic association approach whereby close to 2.4 million SNPs throughout the genome were tested in 183,000 participants to assess the existence of a link with height. “Our team of researchers therefore identified 180 DNA regions, each of which explains a fraction of the normal variation in height in the population. This represents the most important step toward improving our knowledge of the genetic factors that explain why we are all of different height,” said Dr. Joel N. Hirschhorn, professor at Harvard University and the Broad Institute, and co-director of the study.

A large-scale study that opens the door to new research

Because this was one of the largest studies on pangenomic association ever conducted owing to the sheer number of participants assessed, it was possible to test several new hypotheses. “We demonstrated that the genes associated with complex human traits such as height come together in common signalling pathways. In other words, even if genetic variations that influence height are extremely numerous, we’ve observed that there is nothing random about their dispersion in the genome and that these variations are manifest in genes with similar biological functions,” added Dr. Lettre. “In doing so, our study responds to a major criticism against studies on pangenomic association, namely that the identification of great numbers of SNPs linked to a given trait holds little scientific value, since they would usually be randomly dispersed in the genome.” The study of biological signalling pathways identified by the GIANT Consortium thus opens up new possibilities, for example in endocrinology research.

Complex traits, complex genetics

In spite of the scope of the study, the 180 SNPs identified by researchers only explain some 10% of hereditary variation in height – far from the 80% estimated. “Even if studies on pangenomic association are powerful tools, we’re still far from fully understanding how differences between genomes influence traits such as height,” cautions Professor Tim Frayling of the Peninsula Medical School and the University of Exeter, also a collaborator on the study. “We found that a trait such as height is far more complex than we anticipated and that other strategies are necessary to understand how our genetic differences have an impact on individual characteristics such as height or predisposition to illness.”

“Indeed, contrary to so-called simple genetic diseases such as cystic fibrosis and sickle-cell anemia, where a single mutation causes the disease, height is influenced by the sum of hundreds of genetic variations that we all carry in our DNA. Knowing this, if we can understand the genetics of height, we can then apply this knowledge to other complex hereditary human diseases, notably cardiovascular diseases,” concluded Dr. Lettre.

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