Is short stature associated with a 'shortage' of genes?

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New research sifts through the entire genome of thousands of human subjects to look for genetic variation associated with height. The results of the study, published by Cell Press in the December issue of the *American Journal of Human Genetics*, suggest that uncommon genetic deletions are associated with short stature.

Height is a highly heritable trait that is associated with variation in many different genes. "Despite tremendous recent progress in finding common genetic variants associated with height, thus far these variants only explain about 10% of the variation in adult height," explains senior study author, Dr. Joel N Hirschhorn, from Children's Hospital Boston and the Broad Institute. "It has been estimated that about half of height variation could eventually be accounted for by the sorts of variants we've been looking at, so it is possible that other types of genetic variants, such as copy number variants (CNVs), may also contribute to the genetic variation in stature."

Dr. Hirschhorn, co-authors Dr. Yiping Shen and Dr. Andrew Dauber, and their colleagues were interested in looking for associations of human stature with CNVs, something that has not been done before. A CNV is an excess (gain) in genetic material or an absence (deletion) of parts of the genome. Some CNVs are common, meaning that they are observed often in the human genome. Other CNVs are rare or occur with low frequency in the human population.

"To investigate whether CNVs play a role in short or tall stature, we conducted a genome-wide association study of copy number in a cohort of children who had comparative genomic hybridization microarray screening for clinical reasons and we observed an excess of rare deletions in children with short stature," says Dr. Shen. "We extended our findings to a large population-based cohort, and again observed an excess of low frequency deletions in shorter individuals." The findings were not due to known gene deletion syndromes and no significant associations were observed between CNV and tall stature.

Taken together, the results demonstrate that there is a correlation between low frequency genetic deletions and decreasing height. "Our findings strongly support the hypothesis that increasing burden of lower frequency deletions can lead to shorter stature, and suggest that this phenomenon extends to the general population," concludes Dr. Dauber.

Provided by Cell Press