SISG 2018: Genetic Epidemiology

Title: Epigenetic and genetic components of height regulation

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Journal and year: Nature Communications; 2016

Abstract:

Adult height is a highly heritable trait. Here we identified 31.6 million sequence variants by whole-genome sequencing of 8,453 Icelanders and tested them for association with adult height by imputing them into 88,835 Icelanders. Here we discovered 13 novel height associations by testing four different models including parent-of-origin (|β|=0.4–10.6 cm). The minor alleles of three parent-of-origin signals associate with less height only when inherited from the father and are located within imprinted regions (IGF2-H19 and DLK1-MEG3). We also examined the association of these sequence variants in a set of 12,645 Icelanders with birth length measurements. Two of the novel variants, (IGF2-H19 and TET1), show significant association with both adult height and birth length, indicating a role in early growth regulation. Among the parent-of-origin signals, we observed opposing parental effects raising questions about underlying mechanisms. These findings demonstrate that common variations affect human growth by parental imprinting.

Guiding questions:

1. Identify instances of topics we have covered and the role they play in this project. For example, linkage disequilibrium, imputation, phasing.
2. What data are needed to be able to study parent-of-origin associations?
3. For many of the hits, the authors point out prior research that supports their finding. What types of evidence did you find most convincing (i.e. prior GWAS, disease associations, human gene expression and imprinting studies, animal models, etc.)?
4. Can you identify any limitations or concerns with this study? What might you have done differently?
5. What might be next steps based on this study?
6. What are challenges for trying to replicate findings from this study outside of the Icelandic population?
7. What did you find most interesting about this paper?