Vanderbilt Genetics Institute

VANDERBILT UNIVERSITY MEDICAL CENTER

Analysis of Genetic and Environmental Contributions to Lipids Reveals Differential Patterns of Disease Associations in a Large Biobank

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Introduction

- Biological markers are measurable substances found in biospecimens that can indicate the severity or risk of a particular outcome, like disease or infection.
- Blood lipid measurements are important markers in determining an individual's risk of developing cardiovascular and metabolic diseases.
- The variation between people in these biomarkers is due to a combination of both genetics and environment.
- The common variant genetic contribution to each biomarker can be estimated using a polygenic score, which reflects a measurable part of the common genetic contribution to lipid levels.
- Removing variance due to genetics from the overall measured value can approximate the environmental contribution to lipids.
- The resulting residual variance, termed the 'lipid residual' reflects environmental variation and measurement error

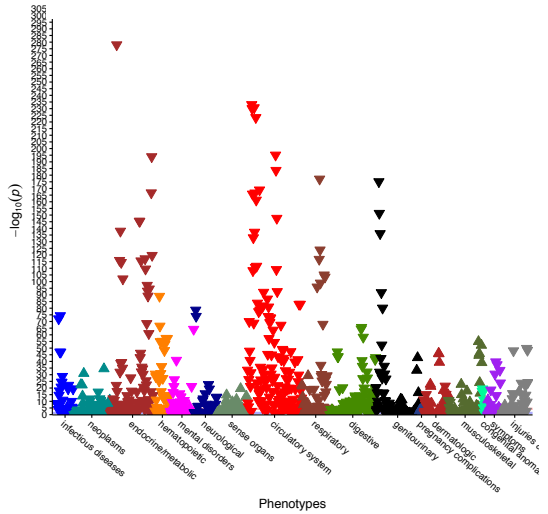

Figure 1: PheWAS plot of HDL residuals

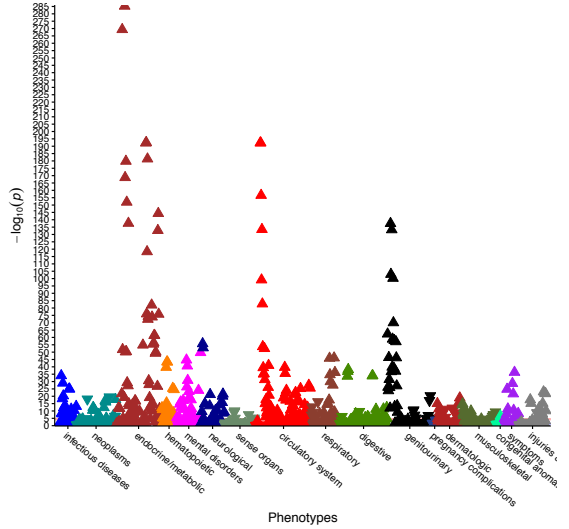

Figure 2: PheWAS plot of Triglycerides residuals

Methods

Calculation of Residuals

- $\text{resid}(\text{Lipid Trait}_{\text{measured}} \sim \text{Lipid Trait}_{\text{PGS}})$
- $\text{Phenotype} \sim \text{Lipid Trait}_{\text{resid}} + \text{Age} + \text{Sex} + \text{PC1...+PC10}$

Results

For 73 and 224 phenotypes significantly associated with Triglycerides and HDL, respectively, the Beta from the residual analysis was significantly greater than the Beta from the median value analysis, suggesting that the PRS is adding variance that might mask disease association with 'environmental' Lipids. For 50 and 201 phenotypes significantly associated with Triglycerides and HDL, respectively, the Beta from the median value analysis was significantly greater in magnitude than the residual association suggesting that the original association may be largely driven by genetic regulation of lipids

Future Directions

We are currently investigating the associations of LDL residuals before and after statin use.

Acknowledgements

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