The placenta serves as the master regulator of the intrauterine environment via nutrient transfer, metabolism, gas exchange, neuroendocrine signaling, growth hormone production, and immunologic surveillance1. Due to strong influences on neonatal health, the placenta is central to the Developmental Origins of Health and Disease (DOHaD) hypothesis: that the *in utero* experience has lifelong impacts on child health by altering developmental programming and influencing risk of common, non-communicable health conditions2. Despite its long-lasting influences on health, the placenta is understudied in large consortia studies of multi-tissue gene regulation3,4. Studying regulatory mechanisms in the placenta underlying biological processes in developmental programming could provide novel insight into health and disease etiology.

* We showed that placental gene expression mediates associations with multiple childhood outcomes and many traits across the life course, namely metabolic traits
* This poses a hypothesis that we can explore through longitudinal GWAS with larger sample sizes
* However, these advances have been made in European ancestry

*Aim 1 will detect gene- and isoform-level expression quantitative trait loci in the placenta through a multi-ancestry mega-analysis.*

*Aim 2 will deconvolve molecular signals from bulk placenta tissue and detect cell-type-shared and -specific QTL signals*.

*Aim 3 will detect susceptibility genes for metabolic traits with differing effects across the early childhood life course.*

The proposed work will develop a novel suite of tools that extends current methodology to integrate GWAS and gene expression data to quantify the influence of distal SNPs on regulation of tissue-specific gene expression and prioritize testable, mechanistic hypotheses for trait associations. These tools will provide the field with accessible software to study genome-wide effects on gene regulation and its impact on complex traits. These methods will also be applied in studies of neuropsychiatric disorders, revealing novel insight into the underlying genetic control of these complex traits. We aim to provide a valuable resource for the wider biological and medical community to fully make use of genome-wide assays of DNA and RNA sequencing, as well as other molecular profiles, that have not been possible due to limitations in methodology.

**References**

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