NIH Award from the National Human Genome Research Institute

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- **Project:** GWA Mapping: Maternal Metabolism-Birth Weight Interactions  
- **Start Date:** September 19, 2009  
- **Total Award Amount:** $65,044

**How the results of this project will benefit society:**

Low and high birth weights are a major cause of neonatal morbidity and mortality, and epidemiological data have established an association between birth weight and later risk of adult metabolic disease. Fetal growth is determined by complex interactions between fetal genes and the maternal uterine environment. Subtle or overt variation in maternal glucose tolerance which is, in part, genetically determined, is related to fetal size at birth. New emerging data suggest that genetic variation in the fetus can impact maternal metabolism.

**The problem the project is trying to solve:**

Given the above, we are hypothesizing that during pregnancy, gene-environment interactions in the context of the maternal-fetal unit impact fetal size at birth and maternal metabolism. To address this hypothesis, we are proposing to perform genome wide association (GWA) mapping on a subset of ~37,000 DNA samples that were collected from mothers and their offspring as part of the NIH-funded Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. HAPO is a multicenter, international study in which high quality phenotypic data related to fetal growth and maternal glucose metabolism has been collected from 25,000 pregnant women of varied racial and socio-demographic backgrounds using standardized protocols that were uniform across centers.

**How the project will work:**

We are proposing to genotype 1,500 infants and their mothers of European descent to accomplish the following specific aims: (1) To apply analytic approaches for conducting GWA mapping studies on quantitative phenotypes related to offspring size at birth (birth weight, ponderal index, head circumference and adiposity) allowing for other known influences such as gestational age, parity, and maternal weight gain. (2) To apply the above approaches to identify genetic variation that impacts maternal glucose tolerance at ~28 weeks of gestation (fasting glucose, glucose during an oral glucose tolerance test, and insulin sensitivity expressed as quantitative traits) allowing for other known influences such as maternal weight gain, parity and age. (3) To examine the interaction between maternal genes, the intrauterine environment, and fetal genes to identify interactions that modulate genetic regulation of size at birth and fetal genetic variation that impacts on maternal glucose tolerance. A replication study will be performed in additional infants and mothers of European descent with follow-up studies also planned in Afro-Caribbeans, Hispanics of Mexican descent and Thais.

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