Genetic Susceptibility to bisphenol A (BPA) and bisphenol A diglycidyl ether (BADGE) and Influences on Metabolic Phenotypes during Pregnancy

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Obesity and metabolic dysfunction have reached epidemic proportions. Susceptibility to obesity and its consequences likely has both genetic and environmental determinants, including intrauterine exposures to environmental contaminants. Bisphenol A (BPA) and its metabolite bisphenol A diglycidyl ether (BADGE) are ubiquitous environmental contaminants that readily cross the placenta during pregnancy, influence adipocyte differentiation and alter glucose and lipid metabolism. Mechanistically, BPA and BADGE antagonize peroxisome proliferator-activated receptor-gamma (PPAR-γ). PPAR-γ has potent insulin-sensitizing and anti-inflammatory properties which are mediated in part through adiponectin, an adipocyte protein.

There is, however, limited research on the influences of BPA/BADGE on adiponectin levels and insulin sensitivity in humans, especially during pregnancy, when the fetus may be uniquely susceptible to alteration of metabolism by environmental contaminants. Studying exposure during pregnancy also allows us to understand response to BPA/BADGE exposure in the context of shared genetic effects, as mother and baby share half of their genes in common. The long-term goal of this research is to identify the influence of environmental contaminants BPA/BADGE on metabolic development during the fetal period and early childhood, and to identify specific genetic variants influencing susceptibility to these contaminants. In this project, we will use a cohort of 50 mother-infant pairs to explore the associations between BPA/BADGE and adiponectin in the mother and infant, and to establish a genetic model for susceptibility to BPA/BADGE. We hypothesize that exposure to BPA/BADGE during pregnancy increases the risk of metabolic dysfunction in both mother and infant, and that genetics alter the sensitivity to these compounds.