

Tiffany M. Newman, BS

Department of Surgery- Hypertension and Vascular Research Center

PhD Student

Maternal Macronutrient Consumption Yields Long-Term Outcomes On The Metabolic Health And Microbial Colonization Of Female Offspring

Tiffany M. Newman, BS; Kenysha YJ Clear, BS; Adam S. Wilson; David R. Soto-Pantoja, PhD; Katherine L. Cook, PhD

Maternal diet during pregnancy has been linked to the metabolic syndrome and other health risks in the adult lives of offspring. Nutrition provided to the growing offspring in the fetal environment is determined by the mother's diet, and since nutrition influences gut microbiome diversity, it follows that the gastric microbiome of the offspring should also be impacted by maternal diet. In this study, we use a mouse model to compare the effects of a maternal 60% kcal from fat lard-based diet, a 60% kcal from fat lard+flaxseed oil-based diet, a 60% sucrose high sugar diet, and a 10% fat 11.2% sucrose control diet on the microbiota colonization and metabolic health of female offspring into their adult lives. To accomplish this, dams were placed on these experimental diet 4 weeks before breeding and throughout pregnancy. Female offspring (regardless of maternal diet) were placed on the control diets at weaning for 10 weeks until adulthood. Therefore, these mice only experienced high-fat or high-sugar diets during early life (in utero to weaning). We collected feces from the pregnant dams, female offspring at weaning (3-weeks of age), and again at adulthood after 10 weeks on a control diet. We also measured body weight and performed glucose tolerance testing at weaning and at adulthood. At the end of the study, gonadal fat pad visceral adipose tissue was weighed and snap-frozen for metabolomic analysis. We show that maternal high-fat diet exposure led to persistent, significant changes in female offsprings' body weight and glucose tolerance. Addition of flaxseed oil restored glucose tolerance to that of control diet-exposed animals by adulthood. While exposure to high sugar diet early in life did not regulate female offspring metabolic parameters, the daughters did display increased mammary gland weight at end of study. Our microbiota data from fecal 16S sequencing indicate significant alterations in the gut microbiome as a long-term effect of maternal diet and early life exposure, with each dietary group expressing a unique microbial outcome. Of particular interest, consumption of a high fat lard-based diet led to persistent upregulation of Lachnospiraceae, Ruminococcaceae, and *Clostridium cocleatum* fecal abundance. It has been shown that several bacterial species in the microbiome can have adipogenic effects, a theme that was recapitulated in our model. Metabolomic analysis of visceral adipose tissue harvested from female offspring at adulthood (after 10-weeks on control diet) indicated that maternal consumption of lard+flaxseed oil diet increased microbial-processed metabolite products. We further examined these microbial alterations using a series of ex-vivo experiments to illustrate the influence of microbial metabolites on inflammatory cytokine expression in the visceral adipose tissue. Our data indicate a previously unreported influence of early life exposure to maternal macronutrient intake on the metabolic and microbial health of female offspring.

Supported By: The Chronic Disease Research Fund grant and an American Cancer Society Research Scholar Grant