23 The fetal microbiome is altered in association with maternal diet during gestation

Amanda Prince[1], Derrick Chu[1], Kristen Meyer[1], Jun Ma[1], Karalee Baquero[2], Peter Blundell[2], Tyler Dean[2], Diana Takahashi[2], Jed Friedman[3], Kevin Grove[2], Kjersti Aagaard[1]

[1]Baylor College of Medicine, Houston, TX, [2]Oregon National Primate Research Center, Beaverton, OR, [3]University of Colorado School of Medicine, Aurora, CO

OBJECTIVE: Adverse *in utero* conditions and dysbiosis of the gut microbiome are associated with metabolic disease. Prior studies demonstrate that the gut microbiome is largely influenced by diet, and our previous study shows that maternal diet is associated with persistent dysbiosis of the offspring microbiome at one year of age. Here, we aim to determine if dysbiosis associated with maternal diet exposure can occur *in utero* and can be ameliorated through interventions in our non-human primate model.

STUDY DESIGN: Japanese macaque dams were fed a control (CTR) or high-fat diet (HFD). Additionally, therapeutic interventions using resveratrol (RESV) and diet reversal (REV) were utilized during pregnancy. Dams were socially housed and at gestational day 130 (G130), offspring were delivered by Cesarean, and swabs of the fetal colon and oral cavity were obtained, as well as maternal oral, anal, and vaginal samples (42 samples in total). In a second cohort of animals, offspring were vaginally delivered at term (167 days) and maintained on the maternal diet through weaning (n=21). 16S sequencing for microbial DNA was performed.

RESULTS: We found that the fetal microbiome is significantly altered by maternal CTR versus HFD (p=0.035, Fig A), and Pasteurellaeis is significantly increased with exposure to a maternal HFD ($p<0.05$, Fig B). Additionally, we found that the offspring gut microbiome is altered by maternal dietary exposures at 6 and 10 months of age (Fig A). In agreement with our prior studies, we found that *Campylobacter* was absent when offspring were ever exposed to a HFD ($p<0.05$, Fig B). The microbial metagenomic pathways mirrored and extended these findings, with changes in HFD-driven microbial bile secretion during gestation, tryptophan metabolism during nursing, and butanoate metabolism post-weaning ($p<0.05$, Fig C).

CONCLUSION: Altogether, our data demonstrate that a maternal HFD impacts the developing microbiome *in utero* (fetal data) and these influences have a persistent influence on offspring (6 & 10 months of age). Furthermore, our microbial metabolic pathway data suggest that the footprint of the maternal HFD has both age-specific and long-lasting impacts on the gut microbiome community structure and metabolic function. These pathways may provide novel opportunities to prevent dysbiosis of the microbiome and adult metabolic disease.

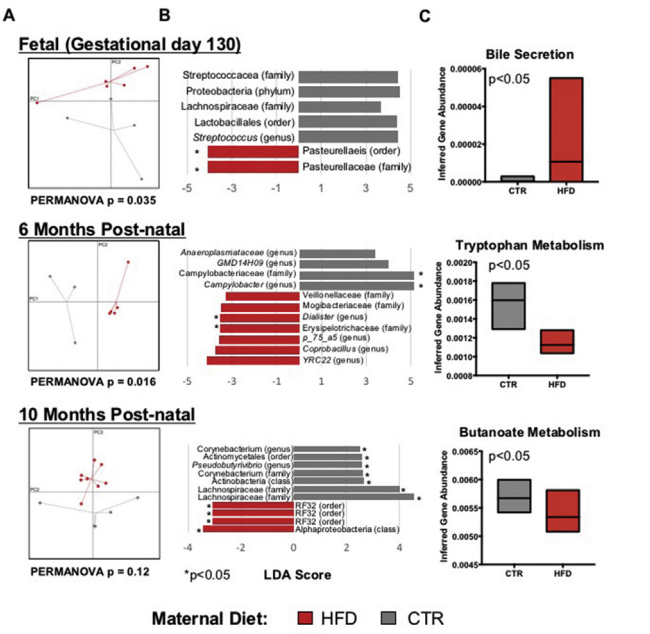

Figure 3: Maternal diet is associated with alterations in the offspring microbiome *in utero* and postnatally. Offspring were exposed to maternal diet during gestation (G130), nursing (6 months), and post-weaning (10 months). (A) PCoA demonstrates significant differences in the fetal microbiome and juvenile gut microbiome associated with maternal dietary exposures. (B) LEfSe analysis reveals significant taxonomical differences in the fetal microbiome and juvenile microbiome associated with maternal diet. (C) Inferred metabolic pathways analyzed by PICRUSt demonstrate significant differences ($p<0.05$) in metabolic pathways associated with maternal dietary exposures during gestation, lactation, and post-weaning.

24 Evidence for the presence and regulation of tenascin-X (TNXB) in pregnancies complicated by preterm birth and intra-amniotic infection (IAI)

Guomao Zhao[1], Emily A. Oliver[2], Kara M. Rood[2], Catalin S. Buhimschi[2], Taryn Summerfield[2], Irina A. Buhimschi[1,2]

[1]Nationwide Children's Hospital, Center for Perinatal Research, Columbus, OH, [2]The Ohio State University College of Medicine, Columbus, OH

OBJECTIVE: TNXB is an extracellular matrix protein primarily found in connective tissue. TNXB regulates fibrillogenesis of collagens I, III, and V, and its expression is stimulated by pro-inflammatory cytokines. This study was conducted to investigate the expression of TNXB in amniotic fluid and reproductive tissues of pregnancies complicated by PPROM and IAI.

STUDY DESIGN: Amniotic fluid was retrieved by clinically indicated amniocenteses from 334 singleton pregnancies. We analyzed the following groups: **1)** 2nd trimester control (2nd-CRL, genetic karyotype), n=34, GA: 19 [17-20w]; **2)** 3rd trimester control (3rd-CRL, lung maturity), n=31, GA: 36 [35-37w]; **3)** rule-out infection, n=269, GA: 27 [24-31w]. Out of the last group, 226 women delivered preterm in the setting of either (+) IAI intact membranes (n=64), (+) IAI PPROM (n= 50), (-) IAI intact membranes (n=64), (-) IAI PPROM (n=48). 43 women had (-) IAI and delivered at term. Levels of TNXB were confirmed by ELISA. Expression of TNXB in placenta, fetal membranes, myometrium and cervix were investigated by immunohistochemistry (IHC) and RT-PCR.

RESULTS: **1)** In women who delivered at term, TNXB amniotic fluid levels were GA regulated with lower levels in the 3rd trimester (r=0.55, P=0.002); **2)** IAI upregulated TNXB levels compared to