BASIC SCIENCE 1

Abstracts 20-30

20 Maternal diet structures the breast milk microbiome in association with human milk oligosaccharides and gut-associated bacteria

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OBJECTIVE: We have previously shown that a high fat maternal diet (HFD) during gestation and lactation has a long-term impact on the offspring gut microbiome. However, the relative contribution of breast milk is unknown. In this study, we sought to determine mechanisms by which diet may modulate composition of the milk microbiota. Specifically, given the role of human milk oligosaccharides (HMOs) in protection against both dysbiosis and necrotizing enterocolitis, we hypothesized that there may be an interaction between maternal HFD, HMOs, and the breast milk microbiome.

STUDY DESIGN: Two dietary treatments were tested in single-blinded cross-over dietary intervention studies of lactating women. The first cohort (n = 7) received a high fat or carbohydrate diet, with a 1-2 week washout period. The second cohort (n = 7) received 60% of their daily caloric intake from either glucose or galactose, with a 1 week washout period. Milk samples collected after each dietary treatment were subjected to 16S metagenomic analysis and HPLC/MS to profile the microbiome and HMO composition, respectively.

RESULTS: High fat versus carbohydrate diet significantly alters the milk microbiome (p = 0.038, Figure A), including significant shifts in several gut-associated taxa (Figure B). High fat diet decreases concentration of sialylated HMOs (p = 0.02, Figure C), and glucose versus galactose diet significantly alters concentration of fucosylated HMOs (p = 0.02, Figure C). Intriguingly, sialylated HMO concentration is significantly correlated with microbiome composition in both dietary cohorts (p = 0.0015, Figure D), suggesting these HMOs play a key role in structuring the milk microbiome.

CONCLUSION: Maternal diet significantly alters the milk microbiome, HMO composition, and abundance of gut-associated taxa. These findings suggest that dietary influence on the milk microbiome is mediated in association with an altered proliferation of bacteria due to changes in sialylated HMO concentration. Additionally, we speculate that shifts in the maternal gut microbiome are translated to the milk microbiome via trafficking of enteric bacteria, resulting in the observed shifts in gut-associated taxa in breast milk.

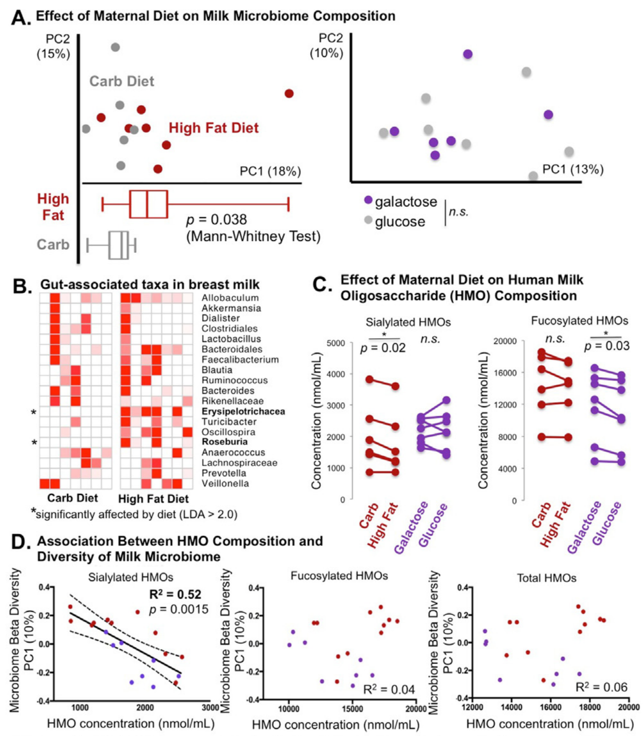

Figure: A. High fat versus carbohydrate diet significantly impacts the composition of the milk microbiome (p = 0.038, Mann-Whitney), while no significant clustering by virtue of glucose versus galactose diet was detected. **B.** Breast milk contains many gut-associated bacteria including two taxa significantly influenced by diet. **C.** High fat versus carb diet significantly alters concentration of sialylated HMOs (p = 0.02, paired t-test) while glucose versus galactose diet significantly alters concentration of fucosylated HMOs (p = 0.03, paired t-test). **D.** Beta diversity of microbiome is significantly correlated with concentration of sialylated HMOs (R^2 = 0.52, p = 0.0015, Pearson correlation) in subjects from both cohorts, but is not correlated with concentration of fucoslylated HMOs nor total HMO concentration, suggesting sialylated HMOs play a key role in structuring the milk microbiome.

21 Sex differences in offspring memory and anxiety in a mouse model of maternal diet-induced obesity

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OBJECTIVE: Maternal obesity (MATOB) is associated with cognitive deficits and increased anxiety in offspring, but underlying mechanisms remain unclear. In our prior work, amniotic fluid and mouse embryonic brain gene expression signatures suggested abnormal fetal hippocampal development, with males (M) more significantly affected by MATOB and maternal pregnancy diet. We sought to validate these findings by testing offspring hippocampal learning/memory in a mouse model of maternal diet-induced obesity.

STUDY DESIGN: Female (F) C57BL/6 mice were fed a 60% high-fat diet (HFD) or a 10% fat control diet (CD) for 12 weeks prior to