HIV EXPOSURE AND HUMAN MILK OLIGOSACCHARIDES MODULATE THE INFANT GUT MICROBIOTA

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BACKGROUND

- HIV-exposed, uninfected (HEU) infants experience almost twice the morbidity and mortality of their HIV-unexposed uninfected (HUU) counterparts.
- Maternal HIV infection is associated with changes in the gut microbiome of HEU.[1]
- There are differences in the human milk oligosaccharide (HMO) composition of breast milk by HIV status.[2]
- HMO are not digested by humans but act as a prebiotic for commensal bacteria.
- It is unknown how these perturbations in maternal HMO impact infant microbiome development, and how HIV status alters this relationship.

METHODS

- Fecal samples collected from infants 1-3 months postpartum in Port-au-Prince, Haiti (see Bender, STM, 2016) were subjected to metagenomic sequencing.
- Sequences identification and host read removal were performed using kraken v1.0 against the NCBI database.
- HMO isoforms were quantified using high-performance liquid chromatography.
- Seventeen unique isoforms were identified.
- All statistical tests were performed in the R environment version 3.5.2. P values evaluated at < 0.05; FDR adjusted for multiple comparisons.

CONCLUSIONS

- Maternal HIV status modulates the associations between HMO profile and infant microbiota.
- This suggests that bacterial utilization of HMO differs in HEU infants, contributing to altered GI and immune development and increased mortality.

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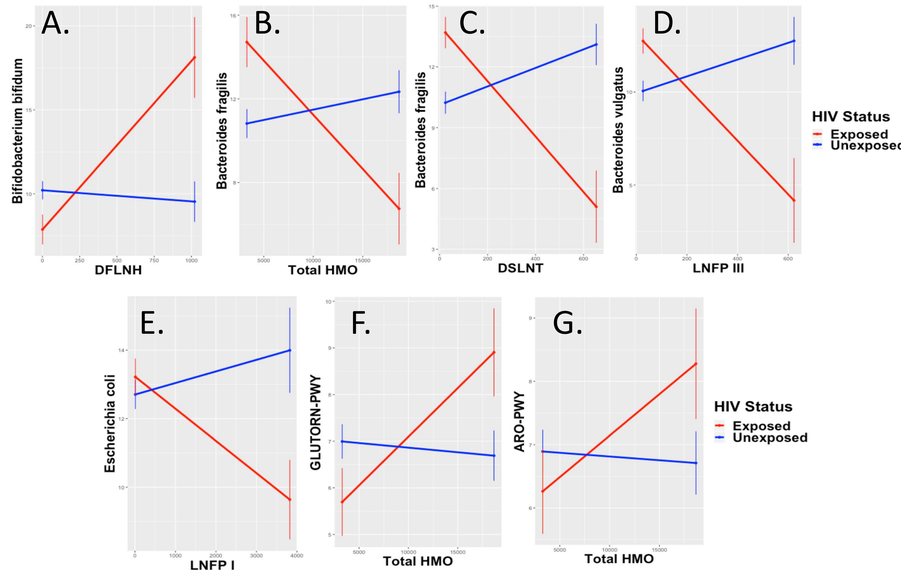
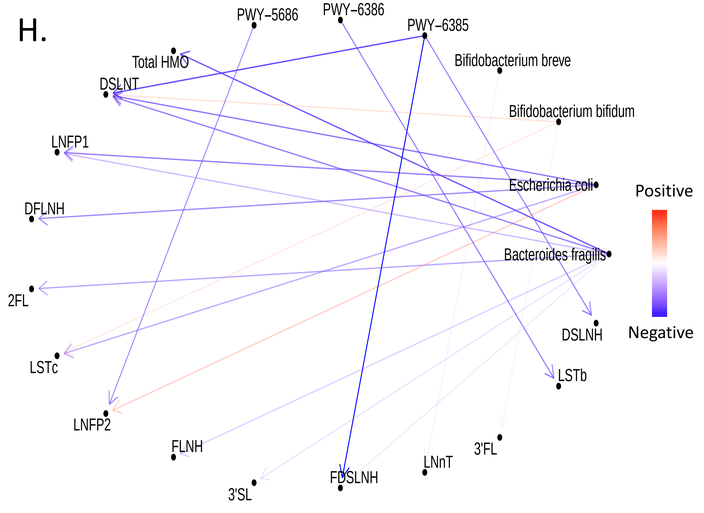
RESULTS

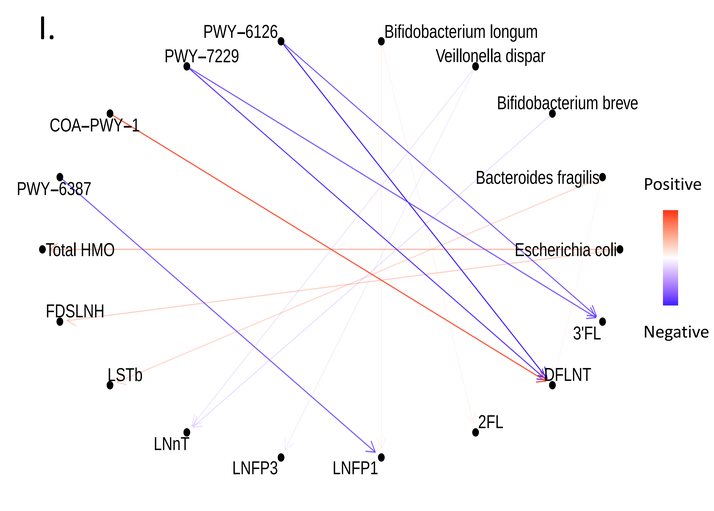
Maternal characteristics	HIV⁺ mothers (n = 17)	HIV⁻ mothers (n = 24)	P
Maternal age (years)	*29.9 (5.57)*	26.9 (7.54)	0.16
Antibiotic use	13 (77)	10 (42)	0.03
Maternal BMI	24.3 (3.84)	21.9 (2.83)	0.03
Exclusive breastfeeding	13 (77)	18 (75)	0.91
CD4 T cell count	609 (259)	N/A	
Infant age (days)	62.3 (46.6)	69.8 (57.2)	0.66
Female sex	8 (47)	13 (54)	0.65
Weight-for-age z score (Underweight)	8 (47)	10 (42)	0.73
Length-for-age z score (Stunted)	7 (41)	5 (21)	0.16

Table 1 - Cohort Characteristics. Overall 41 samples analyzed. No infants received antibiotic treatment, and all mothers were on antiretroviral treatment.





HEU correlations between Taxa/Pathways and HMO



HUU correlations between Taxa/Pathways and HMO

Figures – A-G. Significant negative binomial interaction models of predicted levels of bacterial species by levels of HMO found in the correlation analysis. **H-I.** Network plots of Spearman correlations for HMO, bacterial species and bacterial pathways between HEU **(H)** and HUU **(I).**

PWY-5686: UMP biosynthesis
PWY-6385: peptidoglycan biosynthesis III
PWY-6386: UDP-N-acetylmuramoyl-pentapeptide biosynthesis II
PWY-6387: UDP-N-acetylmuramoyl-pentapeptide biosynthesis I
COA−PWY−1: coenzyme A biosynthesis II
PWY-7229: superpathway of adenosine nucleotides de novo biosynthesis I
PWY-6126: superpathway of adenosine nucleotides de novo biosynthesis II

These differential correlations suggest that bacterial utilization of HMO differs in HEU infants which may, in turn, contribute to altered GI and immune development and increased mortality of HEU infants.