Probiotics and Human Milk Differentially Influence the Gut Microbiome and Risk of Necrotizing Enterocolitis (NEC) in Preterm Pigs

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Background
Necrotizing enterocolitis (NEC) is the leading cause of death from gastrointestinal disease in preterm infants. Although the pathogenesis of NEC is not completely understood, prematurity, formula feeding, and dysbiosis of the intestinal microbiome have all been identified as risk factors for this disease.1 Probiotic administration has been associated with the reduction of NEC incidence in at-risk infants, as they have the potential to prevent dysbiosis.2 Bifidobacterium spp. have been associated with health benefits3 including maturation of the immune system and improvement of intestinal barrier function.

Purpose
The objective of this study was to evaluate the effect of dietary supplementation with Bifidobacterium longum subspecies infantis and a human milk oligosaccharide (HMO), sialyllactose (3%) on the incidence of NEC and the taxonomic composition of the gut microbiome in a preterm piglet model.

Methods
A total of 50 piglets were delivered at 90% gestation. During the 7-day study, piglets were assigned to one of five treatments: (1) Commercially available preterm infant formula (2) donor human milk (DHM), (3) Infant formula and HMO, (4) infant formula and B. infantis, (5) infant formula and B. infantis + HMO. NEC incidence and severity were assessed by evaluation and collection of tissue sections from all segments of the GI tract. The gut microbiome composition was assessed by 16S and whole genome sequencing (WGS) of intestinal contents.

Conclusion
- DHM significantly decreased the incidence of NEC
- Supplementing diet with B. longum subs. infantis alone and with 3% was not sufficient to reduce incidence and severity of NEC
- B. longum abundance negatively correlates with disease suggesting marginal benefits to the host.
- Differential abundance of select bacterial species by diagnosis suggests implications of the microbiome composition in disease

References

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Figure 1. Phenotypic study outcomes: A) Survival curve by treatment; B) NEC incidence by treatment; C) Gross NEC severity score by treatment.

Figure 2. 16S and whole genome sequencing (WGS) of intestinal contents: A) Top 10 genera in small intestinal contents by 16S; B) Top 10 genera in colon contents by 16S; C) Top 10 species in colon contents by WGS.

Figure 3. B. longum abundance and correlation with disease: A) Relative abundance by diagnosis; B) Relative abundance by treatment; C) Correlation of relative abundance with disease severity. *p < 0.05; **p < 0.01

Figure 4. E. coli abundance and correlation with disease by WGS: A) Relative abundance by diagnosis; B) Relative abundance by treatment; C) Correlation of relative abundance with disease severity. *p < 0.01

Figure 5. C. perfringens abundance and correlation with disease by WGS: A) Relative abundance by diagnosis; B) Relative abundance by treatment; C) Correlation of relative abundance with disease severity. *p < 0.01