We hypothesized an association between the preterm gut microbiome which may lead to adverse outcomes. These factors which is often insufficient. requirement for parenteral nutrition, and need for mother’s own milk, management of growth due to their increased antibiotic exposure, Preterm infants in the NICU present unique challenges for clinical Covariates: and HUMAnN2

Data Generation:

Sample Processing

Shotgun sequencing was annotated using MetaPhlAn2: Stool samples (n=2947) were collected longitudinally: Extracted DNA was sequenced via shotgun

Study Design

- **Study Population:** 267 preterm infants from 3 different clinical sites with associated data from birth to hospital discharge.
- **Sample collection:** Stool samples (n=2947) were collected longitudinally from 1 to 174 days of life, from infants with normal growth (GN, n=157), GF (n=102) and infants who died (n=8). See background for GF definition.
- **Sample Processing:** Extracted DNA was sequenced via shotgun metagenomic sequencing at a mean depth of 28,390,685 sequences.
- **Data Generation:** Shotgun sequencing was annotated using MetaPhlAn2 and HUMAnN2 (2, 3).
- **Covariates:** Growth Status, Clinical Sites, Probiotic (yes/no), Sepsis, Necrotizing Enterocolitis, Mode of Birth, Gender, Gestational Age at Birth, Post Menstrual Age.

Background

- Prematurity in the NICU present unique challenges for clinical management of growth due to increased antibiotic exposure, requirement for parenteral nutrition, and need for mother’s own milk, which is often insufficient.
- These factors are associated with growth failure (GF), defined as a birth-to-discharge weight z-score decline of ≥1.2.
- The developing gut microbiome is thus perturbed in preterm infants, the developing gut microbiome is thus perturbed in preterm infants, discordant with full-term data. One hypothesis is that while the growth failure, with ~1.64 Relative Risk Ratio after the first 30 DOL. Further exploration of the association between PGCTs and GF using robust statistical techniques to incorporate all samples.

Data Set

- **Mode of Delivery:** Vaginal (41.5%), C-section (58.5%).
- **Gestation Age at Birth:** 32 weeks (21.4%), 34 weeks (28.7%), 36 weeks (31.4%).
- **Distribution of samples:** 32 weeks (21.4%), 34 weeks (28.7%), 36 weeks (31.4%).

Association Between PGCTs and Growth Failure

- We separated samples into time bins - grouped by PGCTs, PGCT-1 vs the others, and used percent growth normal to calculate the relative risk (RR) of being GF vs GN in the different time windows.
- Multiple testing correction of P-values with Benjamini-Hochberg (BH) FDR.
- We find that infants in PGCT-1 are significantly more likely to have growth failure, with ~1.64 Relative Risk Ratio more than the first 30 DOL.

Next Steps/ Future Work

- Further exploration of the association between PGCTs and GF using robust statistical techniques to incorporate all samples.
- Further investigation of PGCT-1, as it has a strong association with growth failure.

Conclusions

- Preliminary results demonstrate the potential to define distinct gut bacterial community types in preterm infants, which may have value for predicting growth status and informing clinical care to enhance growth.
- Further work is needed to validate these findings and explore if modulating the gut microbiome in the first 30 days of life can improve growth outcomes in preterm infants.
- The bacterial species that were enriched in PGCT-1 include several pathobionts (without proof/claim of ‘causality’) for ex: *Enterococcus_faecalis*, *Escherichia_coli*, *Staphylococcus_epidermidis*, and others.

**References**


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**Results**

**Dirichlet Multinomial Mixtures Identified Six Preterm Gut Community Types**

- Dirichlet multimonial mixtures (DMM) was applied to cluster samples and identified six distinct microbiome “preterm gut community types” (PGCTs) based on the overall bacterial profiles (4).
- PGCTs are numbered 1-6 according to the average age of samples within each PGCT, with PGCT-1 consisting of the earliest samples.
- The bacterial species that were enriched in PGCT contain the least number of species and has the lowest Shannon diversity.

**Covariates:**

- **Study Population:** 267 preterm infants from 3 different clinical sites with associated data from birth to hospital discharge.
- **Sample collection:** Stool samples (n=2947) were collected longitudinally from 1 to 174 days of life, from infants with normal growth (GN, n=157), GF (n=102) and infants who died (n=8). See background for GF definition.
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**Next Steps/ Future Work**

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**References**