Microbial Metabolic Biogeography of the Murine Gastro Intestinal tract in the Context of Aging

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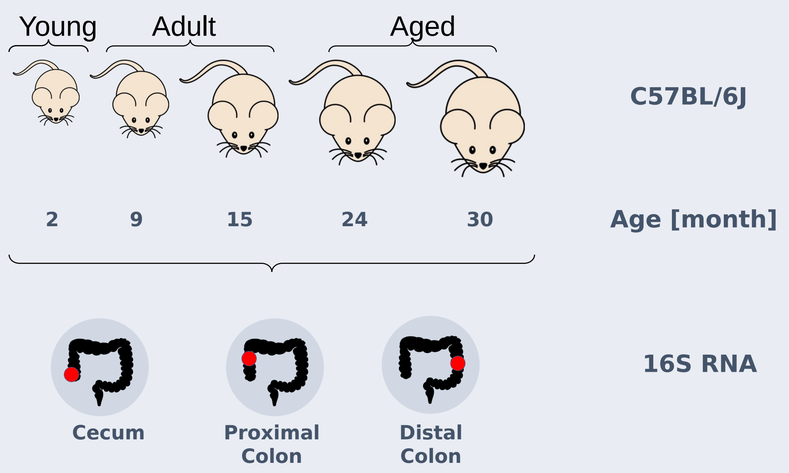
Introduction

- Fecal based sampling techniques do not capture the taxonomic and functional complexity of the entire GI tract
- A more nuanced understanding of the GI microbiota is required to understand its ecology and niche specificity
- Little is know about the connection between biogeography and aging

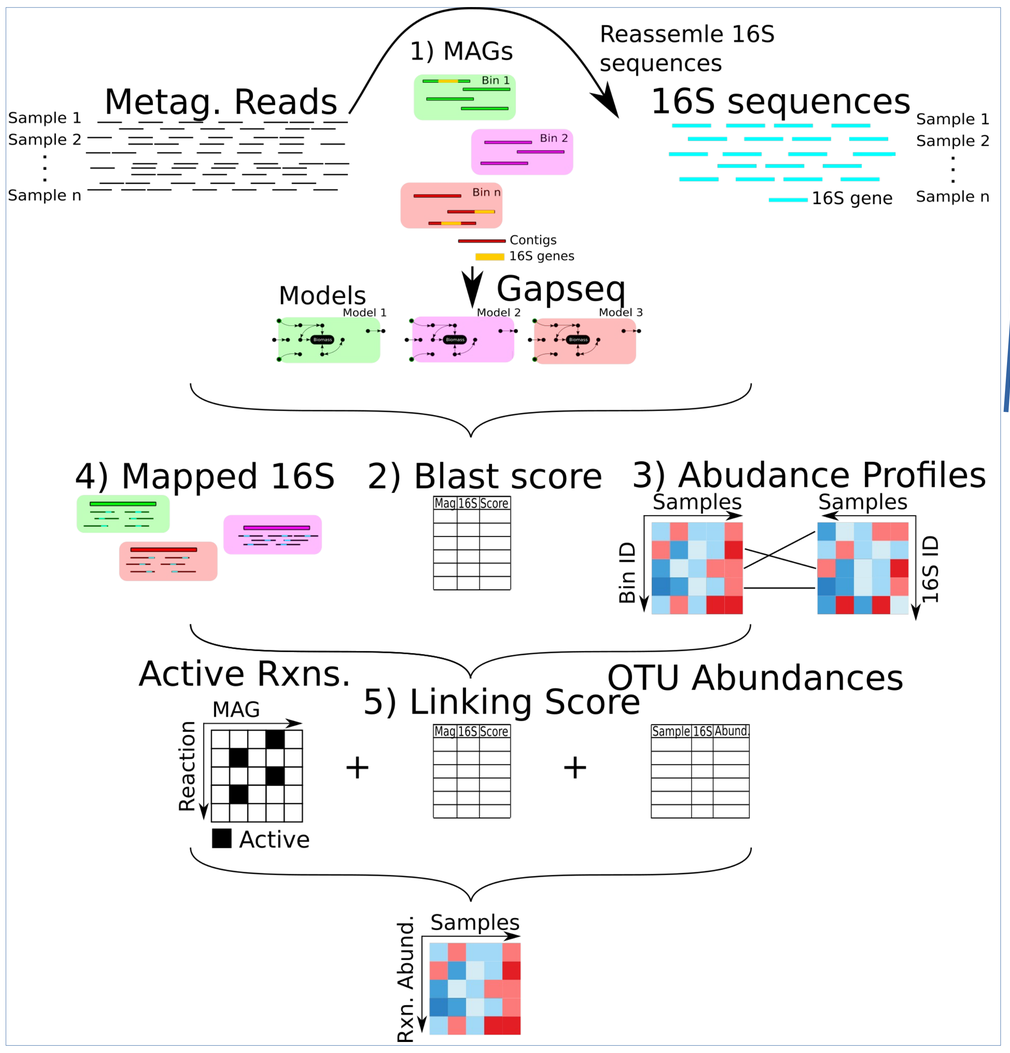
Goals

- Establish a pipeline to connect 16S information to metabolic models
- Investigate taxonomic and functional differences between the gastrointestinal sites through different age groups



Future work

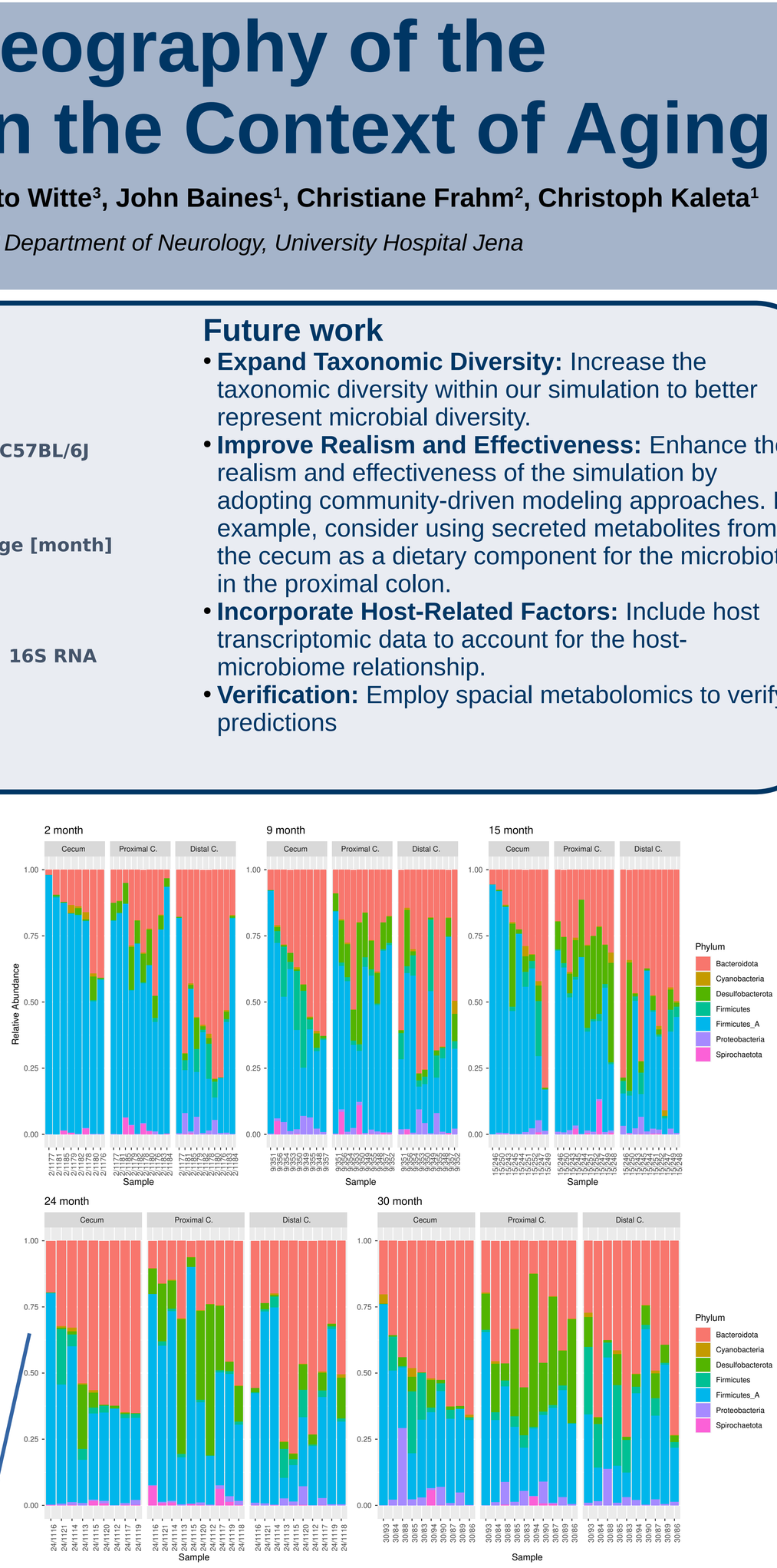
- **Expand Taxonomic Diversity:** Increase the taxonomic diversity within our simulation to better represent microbial diversity.
- **Improve Realism and Effectiveness:** Enhance the realism and effectiveness of the simulation by adopting community-driven modeling approaches. For example, consider using secreted metabolites from the cecum as a dietary component for the microbiota in the proximal colon.
- **Incorporate Host-Related Factors:** Include host transcriptomic data to account for the host-microbiome relationship.
- **Verification:** Employ spacial metabolomics to verify predictions



1. 16S-Model linking

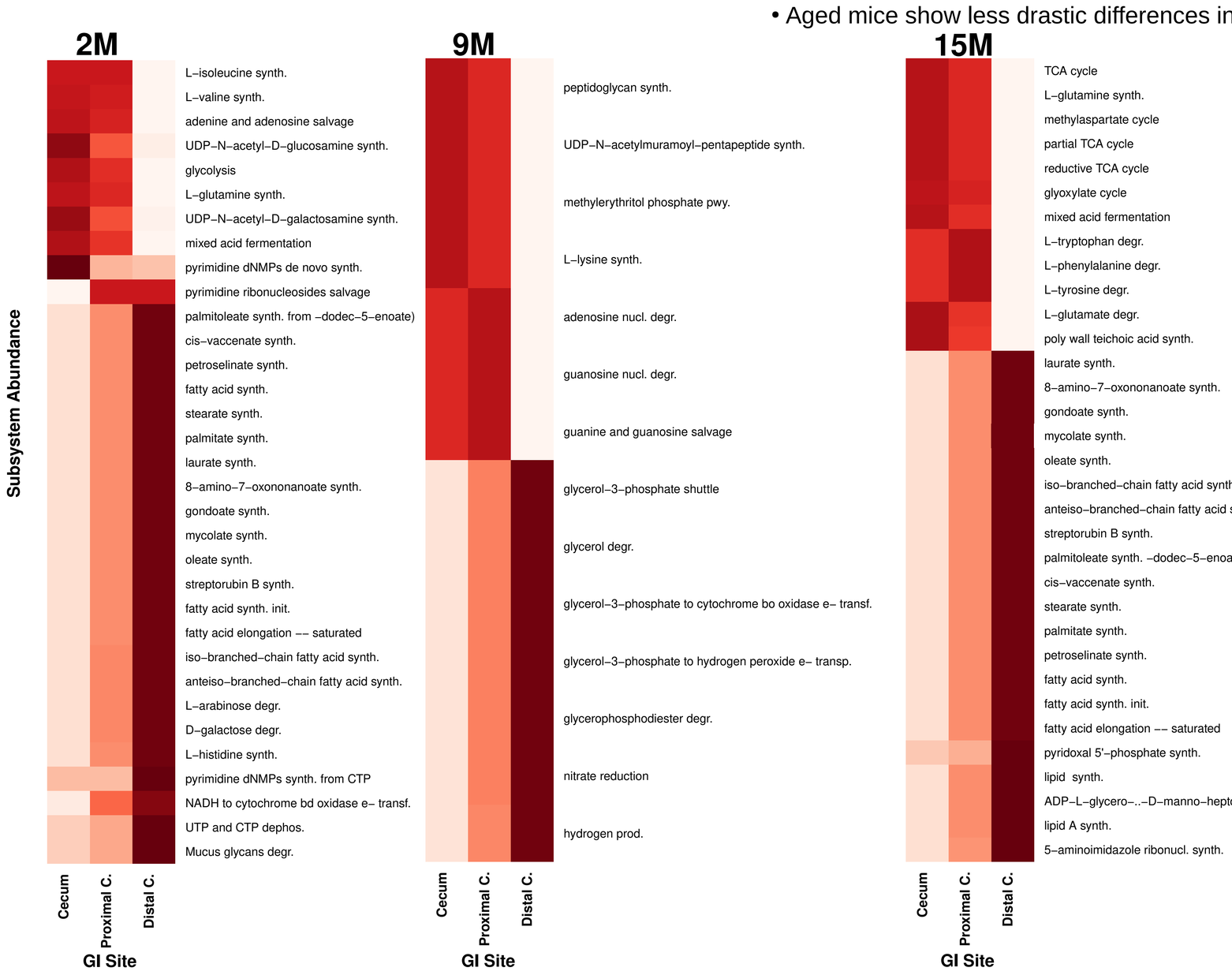
- Enables the linking of taxonomic information (16S) to functional information (metabolic models)
- Based on an approach from *Lesker et al, 2020* that links 16S to MAGs

1) Dedicated assembly of 16S genes
2) Identifying 16S genes in MAGs (Blast)
3) Correlating 16S and MAG abundances across samples
4) Map 16S to MAGs
5) Link all this information into a MAG-16S linking score. Ultimately use this to link 16S to metabolic models created from the MAGs



2. GI Taxonomy

- Increasing rel. abundance of *Bacteroidota* from the cecum to the distal c. in young and adult mice
- Increased rel. abundance of *Desulfobacterota* in the proximal C. across all age groups compared to the other sites
- Aged mice show less drastic differences in rel. *Bacteroidota* abundance



3. Functional enrichment

- First three age groups show different region-specific functions
- No functional differences along the GI tract could be detected in 24 and 30 months old
- 2 month old mice show increased mucin glycan degradation in the distal colon
- Amino acid synthesis more active in the cecum and proximal c. of young mice
- Amino acid degradation more active in the cecum and proximal c. of the GI tract in 15 month old
- Increased (long) fatty acid synthesis along the GI tract in 2 and 15 months old
- Mixed acid fermentation (SCFA production) most active in the beginning of the GI tract in 2 and 15 months old

4. Results

- Established and verified a Snakemake based pipeline to connect metabolic models and 16S information
- The three GI sites show clear functional and taxonomic differences in young and adolescent mice
- No functional differences detectable in 24 and 30 month old mice
- Mixed acid fermentation (SCFA production) most active in the beginning of the GI tract in 2 and 15 months

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