Development of Differing Complex Microbiota in CD1 Mice

Veterinary Research Scholars Program
University of Missouri

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MMRRC Mutant Mouse Resource & Research Centers

Background

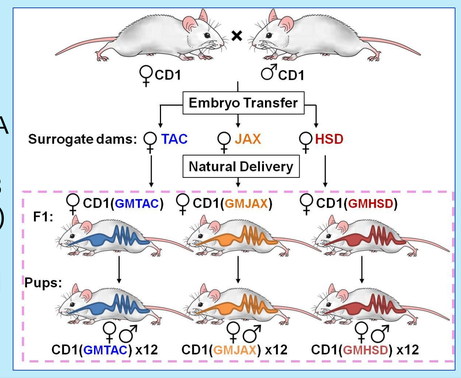
- Differences in gut microbiota (GM) have been shown to modulate many mouse models of disease including colorectal cancer, inflammatory bowel disease, and neurological disorders
- Little is known about early life mouse GM and how early differences in composition and diversity impact disease models

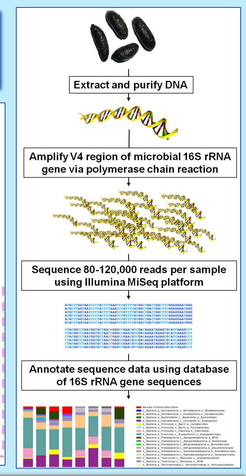
Hypothesis

- Pups will first be colonized with maternal *Firmicutes* and *Bacteroidetes*
- Diversity will increase with age until stabilizing at adulthood
- Pups with Harlan (HSD) GM will have higher diversity and richness than Jackson (JAX) and Taconic (TAC) GM profiles

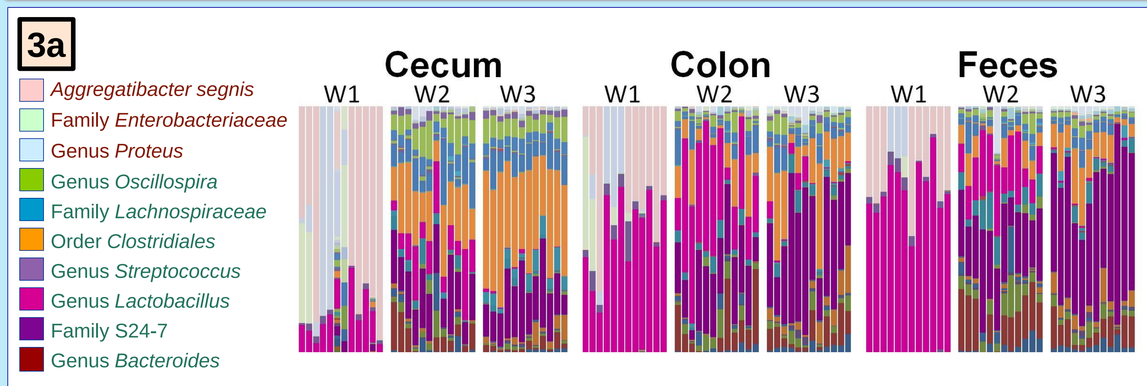
Methods

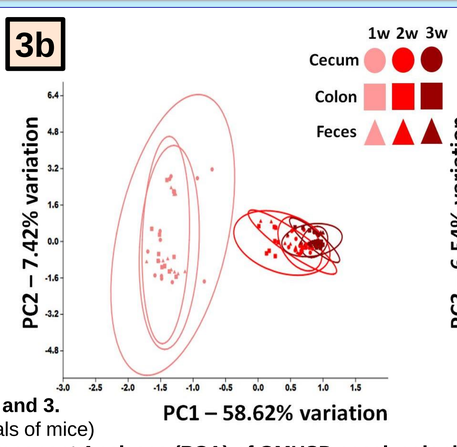
- Obtained rederived CD1 mothers with designated GM profiles
- Extracted and sequenced DNA from cecal, colonic, and fecal samples from pups 1, 2, and 3 weeks of age (n=12/GM/week)
- Performed statistical analysis using PERMANOVA, Principal Component Analysis (PCA) and 3-way ANOVA

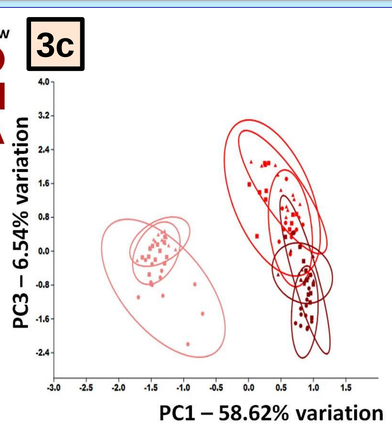




Development in CD1 Mice with Harlan (HSD) GM Profile







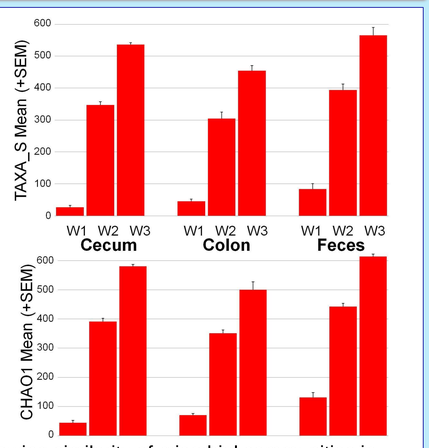
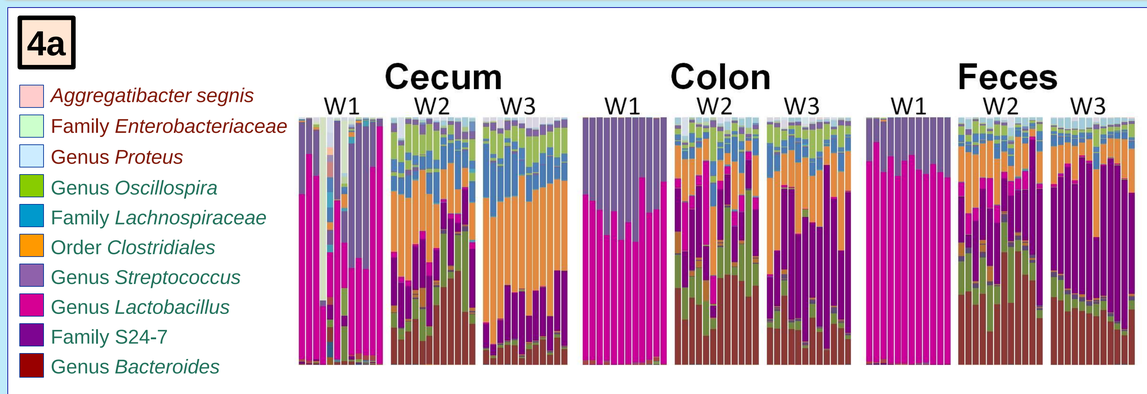
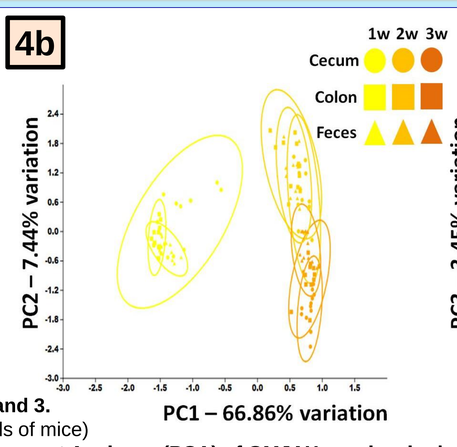
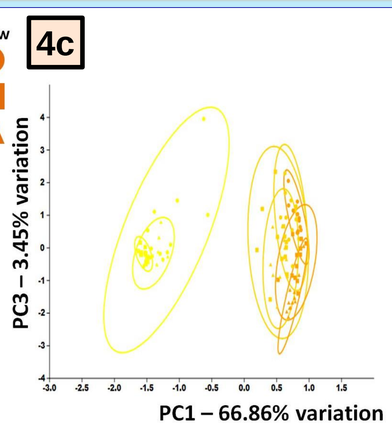


Fig 3a Stacked bar chart of microbiota composition of cecal, colonic, and fecal contents in GMHSD mice at weeks 1, 2, and 3. Data represents Operational Taxonomic Unit (OTU) level analysis with *Bacteroidetes* and *Firmicutes* phlya (common commensals of mice) represented in bright colors and *Proteobacteria* phyla (includes possible pathobionts) in pastels. **Figs 3b and 3c Principal Component Analyses (PCA) of GMHSD cecal, colonic, and fecal contents at 1, 2, and 3 weeks of age** showing similarity of microbial communities in shared sample type and host age**.** Circles represent 95% confidence intervals. **Fig 3d TAXA_S index representing richness between cecal, colonic, and fecal contents at 1, 2, and 3 weeks. Fig 3e CHAO1 index representing diversity (richness + distribution) for cecal, colonic, and fecal samples at 1, 2, and 3 weeks of age.** Bars represent mean + standard error of the mean (SEM); significant ($p < 0.05$) main effects detected for GM, sample site, and time via 3-way ANOVA.

Development in CD1 Mice with Jackson (JAX) GM Profile







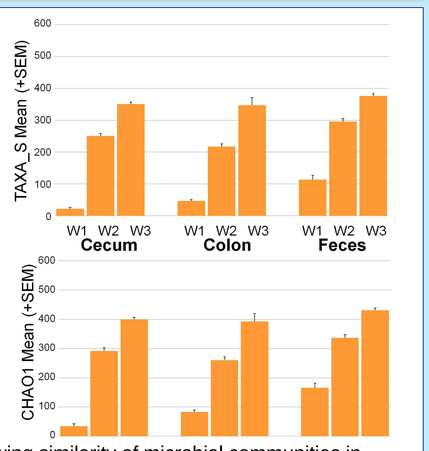
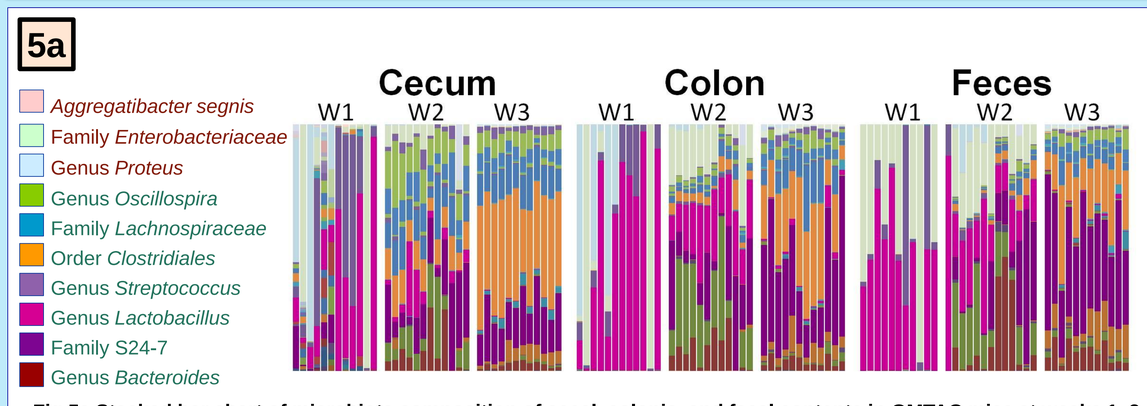
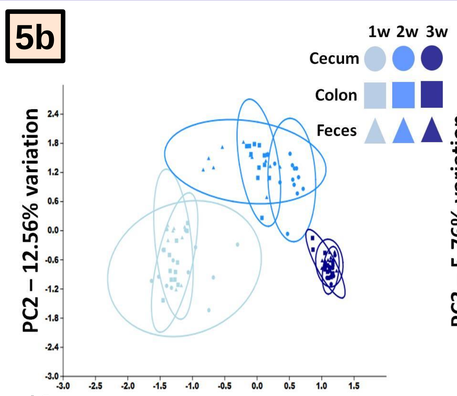
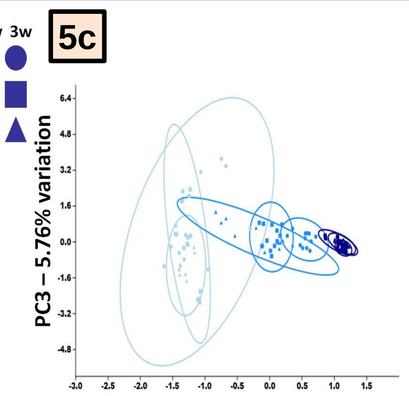


Fig 4a Stacked bar chart of microbiota composition of cecal, colonic, and fecal contents in GMJAX mice at weeks 1, 2, and 3. Data represents Operational Taxonomic Unit (OTU) level analysis with *Bacteroidetes* and *Firmicutes* phlya (common commensals of mice) represented in bright colors and *Proteobacteria* phyla (includes possible pathobionts) in pastels. **Figs 4b and 4c Principal Component Analyses (PCA) of GMJAX cecal, colonic, and fecal contents at 1, 2, and 3 weeks of age** showing similarity of microbial communities in shared sample type and host age**.** Circles represent 95% confidence intervals. **Fig 4d TAXA_S index representing richness between cecal, colonic, and fecal contents at 1, 2, and 3 weeks. Fig 4e CHAO1 index representing diversity (richness + distribution) for cecal, colonic, and fecal samples at 1, 2, and 3 weeks of age.** Bars represent mean + standard error of the mean (SEM); significant ($p < 0.05$) main effects detected for GM, sample site, and time via 3-way ANOVA.

Development in CD1 Mice with Taconic (TAC) GM Profile







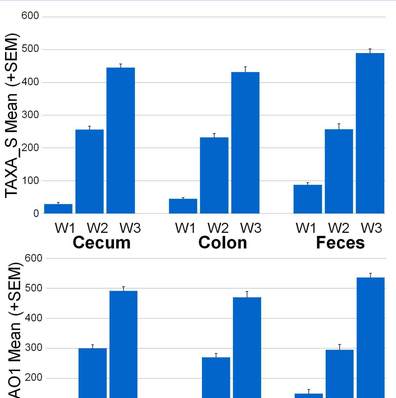


Fig 5a Stacked bar chart of microbiota composition of cecal, colonic, and fecal contents in GMTAC mice at weeks 1, 2, and 3. Data represents Operational Taxonomic Unit (OTU) level analysis with *Bacteroidetes* and *Firmicutes* phlya (common commensals of mice) represented in bright colors and *Proteobacteria* phyla (includes possible pathobionts) in pastels. **Figs 5b and 5c Principal Component Analyses (PCA) of GMTAC cecal, colonic, and fecal contents at 1, 2, and 3 weeks of age** showing similarity of microbial communities in shared sample type and host age**.** Circles represent 95% confidence intervals. **Fig 5d TAXA_S index representing richness between cecal, colonic, and fecal contents at 1, 2, and 3 weeks. Fig 5e CHAO1 index representing diversity (richness + distribution) for cecal, colonic, and fecal samples at 1, 2, and 3 weeks of age.** Bars represent mean + standard error of the mean (SEM); significant ($p < 0.05$) main effects detected for GM, sample site, and time via 3-way ANOVA.

Future Directions

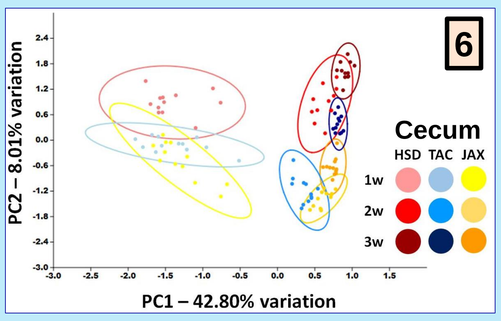


Fig 6 PCA comparing cecal contents of GM profiles at 1, 2, and 3 weeks of age. Circles represent 95% confidence intervals.

- Determine how complex vs. simple GM profiles impact neurological development in mice
- Determine whether neonatal GM modulates tolerance in adulthood
- Determine how cecal GM seeds the colon
- Assess small intestinal GM
- Determine impacts of GM ontogeny on mucosal immune system development

Conclusions

- While *Firmicutes* and *Bacteroidetes* predominated most samples, *Proteobacteria* outweighed both phyla in GMHSD week 1 neonates.
- The cecal, colonic, and fecal GM increased in richness and diversity with age
- Mice previously found to harbor a more complex microbiota in adulthood (GMHSD) had more diversity and richness than mice with simpler profiles (GMJAX, GMTAC).
- Compositionally, GM profiles are the markedly dissimilar at week 1 of age but converge towards adulthood.

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