RE-INTRODUCTION OF MICROBIOTA IN DYSBIOTIC IL-10 KNOCKOUT MICE EFFECTS HOST IMMUNITY, MICROBIAL COMPOSITION, AND FUNCTION

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Objectives: The microbiota has profound influence on the host through interactions with the immune system early in host development. These interactions are crucial in understanding complex autoimmune diseases, such as Inflammatory Bowel Disease (IBD). Here, we examined how re-introducing a microbiota to dysbiotic IL-10 knockout mice during development impacted outcomes of colitis, host immune responses and microbial functional changes.

Methods: Vertically transmitted dysbiotic pups received fecal microbiota transplantation (FMT) from control mice, at 2, 3, and 8 weeks after birth. After 23 weeks, remaining mice were supplemented with 2.5% dextran sulfate sodium to induce colitis.

Results: Colon histology revealed mice receiving FMT displayed less colon inflammation than mice with no gavage. Serum cytokine levels for IL-2 and IL-17 showed significant increase in mice with FMT indicating probable immune education. We assembled 190 non-redundant Metagenome-Assembled Genomes (MAGs) from pup fecal content and highlighted microbial community differences in FMT mice compared to dysbiotic groups. *Akkermansia muciniphila* was highly detected in all mice regardless of dysbiosis, while *Enterococcus sp.* and *Enterobacteriaceae sp*. were highly detected in dysbiotic mice only. These MAGs all shared a large number of antimicrobial resistance genes. The *Enterobacteriaceae sp*. displayed several stress response genes such as osmotic protectant ABC transporters, lipopolysaccharide assembly, and multiple superoxide dismutases, suggesting dysbiotic mice did not maintain gut homeostasis. Correlation analysis between MAG detection and host gene expression revealed two MAGs in the Enterobacteriaceae family strongly correlate with increased host expression of the *CSAD* gene, a cysteine decarboxylase. This gene is responsible for uptake and breakdown of cysteine in the host, suggesting the potential of these MAGs to utilize host L-cysteine.

Conclusions: In dysbiotic mice, an increase in colon inflammation was seen along with an increase in potentially pathogenic microbes were shown. These MAGs showed the potential to persist in the dysbiotic gut, while utilizing host resources, without traditional infection of the colon as seen in serum cytokines.