The incidence of bloodstream infections (BSIs) has increased over time, particularly among patients with immunocompromised or critical care conditions. Pseudomonas aeruginosa (PA) is a significant cause of bloodstream infections (bacteremia), pneumonia, and urinary tract infection. PA bacteremia is a significant cause of morbidity and mortality, especially in immunocompromised patients; however, little is known about the infection dynamics of PA bacteremia. These dynamics are influenced by the host immune system, the microbiome, and the environment.

Methods. We utilized animal modeling in conjunction with sequencing technology to dissect the infection dynamics of PA bacteremia. In parallel, PARL012 engineered to express the luciferase cassette was used to track PA in live mice over time using the IVIS imaging system. STAMP (sequence tag-based analysis of microbial populations) analysis was then applied to define the population dynamics of PA bloodstream infection.

Results. Bacterial enumeration and IVIS imaging revealed that systemically infected mice have a focus of bacterial expansion in their gallbladders (GB). Surprisingly, the same mice also shed PA in their gastrointestinal tract (GI), a phenomenon previously appreciated following bloodstream infection. Finally, STAMP analysis revealed that (1) PA experiences a severe in vivo bottleneck when trafficking to the GI, (2) the population in the GB expands tremendously during infection and (3) this population is ultimately the source of excreted bacteria in the GI tract.

Conclusions. Our research, using dynamic models, provides the first evidence that the GB acts as a sanctuary site for PA replication following systemic infection and links replication with fecal excretion. Fecal excretion of PA from hospitalized patients is observed, but the direct link between acute infection, GI shedding, and transmission remains unclear. Our observations have significant implications on understanding how PA evades initial host clearance, the identity of protected expansion niches, and how PA might exit the human host in the healthcare environment facilitating a transmission event.

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2567. Effect of Broad vs. Narrow-Spectrum Clostridioides difficile Treatment on Human Stool Bile Acid Composition Over Time

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Background. Secondary bile acid production by a diverse commensal flora may be a critical factor in preventing recurrence of Clostridioides difficile infection (CDI). Key enzymes involved are bacterial-encoded bile salt hydrolases (BSHs), felt to be “gatekeepers” to secondary bile acid synthesis. Ridinilazole, a novel narrow-spectrum drug for CDI, demonstrated superior sustained clinical response compared with vancomycin in Phase 2. Longitudinal sampling during this trial allowed for assessment of metabolites differentially present in stools during/after therapy with either broad or narrow-spectrum anti-CDI agent. Previous work characterizing subject’s fecal microbiota in this trial showed that unlike vancomycin, ridinilazole has little effect on commensal flora during and after therapy. We hypothesized that ridinilazole’s microbiota-preserving effect is associated with lack of accumulation of conjugated primary bile acids and/or reaccumulation/persistence of secondary bile acids over the course of CDI treatment, when compared with vancomycin-treated subjects. Furthermore, we hypothesized that we would observe correlations between bile acid profiles and predicted BSH gene abundances.

Methods. Sequential stool samples were obtained from 44 subjects treated with either ridinilazole or vancomycin (22 in each arm), ranging from time of CDI diagnosis, at end-of-therapy, and up to 40 days after diagnosis. Bile acids were quantitated by liquid chromatography-mass spectrometry. Using the PICRUSt algorithm, metagenomic predictions of BSH gene abundances were performed.

Results. Stool bile acid compositions differed between ridinilazole-treated and vancomycin-treated subjects at end-of-therapy. In vancomycin-treated subjects, stool composition became dominated by conjugated primary bile acids and/or reaccumulation/persistence of secondary bile acids over the course of CDI treatment, when compared with vancomycin-treated subjects. Furthermore, we hypothesized that we would observe correlations between bile acid profiles and predicted BSH gene abundances.

Conclusion. Microbiota-preserving CDI treatment with ridinilazole preserves bile acid composition, which may decrease likelihood of recurrence.

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Infections (CDI) result from antibiotic use and cause severe diarrhea (C. difficile-associated diarrhea, CDAD) which is life-threatening and costly. A specific probiotic containing Lactobacillus acidophilus CL1285, L. casei LC80R and Rhamnus CLR2 (Bio-K+) has demonstrated benefits in preventing CDI and has a strong inhibitory effect on the growth of several nosocomial C. difficile strains in vitro. Many Lactobacilli can inhibit CD growth though lactic acidification. Here, we have investigated novel acid-independent mechanisms by which these strains impair C. difficile virulence.

**Methods.** The hypervirulent strain C. difficile R20291 was co-cultured anaerobically with Bio-K+ probiotic strains in various media and glucose concentrations (5 g/L, 3 g/L, 0 g/L), for 24 hours at 37°C. Parameters such as Log CFU, pH, Toxin A and B, cell cytotoxicity were measured. Statistical comparisons using ANOVA one-way was performed in order to determine whether the groups were significantly different.

**Results.** At 5 g/L glucose, no C. difficile toxin was produced and co-culture with these lactobacilli resulted in potent acidification and growth inhibition. At 3 g/L glucose, C. difficile toxin production occurred and acidification by the lactobacilli resulted in growth inhibition as well as >99% reduced Toxin A and B production. In the absence of glucose and a starting pH of 7.0, TY broth, the lactobacilli did not acidify the medium and C. difficile growth was normal yet Toxin A and B production was partially reduced at, 20% and 41% lower. Toxin B from the supernatant of C. difficile grown in TY was cytotoxic to human fibroblast cells, but this was less cytotoxic when co-cultured with the Lactobacilli.

**Conclusion.** These results suggest that the combination of L. acidophilus CL1285, L. casei LC80R and Rhamnus CLR2 interferes with C. difficile pathogenesis through: 1) inhibition of C. difficile growth (via lactic acid secretion), 2) reduced toxin A/B synthesis and (3) toxin neutralization. These results might explain the strain specificity of Bio-K+ probiotic bacteria in potentially preventing C. difficile-associated diarrhea in antibiotic treated patients.

**Table 1.** In vitro model of Clotstridoides difficile R20291 (CD) growth kinetic after 24h in co-culture with or without Lactobacillus acidophilus CL1285, L. casei LC80R and Rhamnus CLR2 (LB) in RCM (Sg/L), BHI (Sp/L) and TY (0 g/L) medium. Log. (CFU/ml), pH and toxin A and B concentration (ng/CFU) were measured in all assays. All experiments were carried out in triplicate.

**Disclosures.** All authors: No reported disclosures.

**Figure 1: Relative Abundance of A Priori Bacteria Significantly Associated with aGvHD at Timepoint T1.**

**Figure 2: Gene Richness at Timepoint T1 in Myeloblastoid vs. Non-Myeloblastoid aHSCT Recipients**

**Figure 3: Heat Map of Relative Abundance of A Priori Bacteria per Conditioning Group and Timepoint**

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