264. Microbiota and Associations with Treatment Outcome in Fecal Microbiota Transplantation

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Background. Fecal microbiota transplantation (FMT) can be an effective treatment of recurrent Clostridium difficile infection (CDI), although nonresponsiveness to treatment remains poorly understood. Here we examine the bacterial composition of stool from FMT recipients using culture-independent methods to identify associations between bacterial community structure, recipient colonization status (FMT administration [colonoscopy or freeze-dried encapsulated FMT capsules]), treatment outcome and donor. We hypothesized that multiple community structures could be associated with and may better define treatment outcome.

Methods. We tested this hypothesis by analyzing bacterial composition profiles and their association with treatment outcome. Statistical analyses were performed using pairwise t-test statistics on 16S rRNA gene sequences (165) from 21 individuals (seven male, 14 female, median 68 years) with recurrent CDI prior to and after FMT. Successful endpoint was defined as no relapse of C. difficile associated diarrhea during 12 weeks post-FMT. There were 17 successes (four colonoscopy, 13 freeze-dried encapsulated FMT capsules) and four failures (all capsules). Analyses of 16S profiles included permutational analysis of variance (PERMANOVA) and linear regression models applied to bacterial abundances and diversity (as responses).

Results. Significant differences were determined between pre- and post-FMT success and failure groups (16S t-test, P < 0.01) across 19 of the 25 most abundant taxa. Of the five most abundant taxa, Enterobacteriaceae and Enterococcus Stigella decreased significantly in successful outcomes, while Faecalibacterium, Blautia, and Bacteroides increased. However, variation in individual composition was also significant suggesting that multiple profiles represent successful outcomes.

Conclusion. Increases in microbiota diversity are generally achieved in successful FMT regardless of administration route, although more than one bacterial composition profile can be identified.

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265. Metabolic Interactions Drive Staphylococcus aureus Adaptation to the Skin

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Background. Staphylococcus aureus is the most common pathogen causing skin and soft-tissue infection and poses a particular problem to patients with atopic dermatitis who have increased colonization and infection rates. S. aureus is a versatile pathogen that adapts to the relatively hypoxic environment of the skin, although the underlying mechanisms of adaptation remain unclear. We hypothesized that adaptation to the skin is largely driven by metabolic interactions between S. aureus and keratinocytes.

Methods. We characterized 10 clinical S. aureus isolates obtained from individual patients with atopic dermatitis to understand dynamic metabolic changes and interactions. isolates were cultured on blood agar plates for 48 hours and mixed at a ratio of 1:1 with normal healthy human skin keratinocytes in tissue culture wells. After 30 days of co-culture, metabolic analysis of keratinocytes and bacterial isolates was performed using liquid chromatography mass spectrometry (LCMS).

Results. Over a period of 30 days, 1:1 mixtures of S. aureus and skin keratinocytes were studied and metabolic changes were observed. LCMS analysis revealed that metabolic adaptation and pathogenesis of S. aureus are driven by metabolic interactions with keratinocytes. This finding was consistent across all 10 clinical isolates, which showed increased metabolic flexibility and adaptation to the skin environment. We also observed a decrease in the expression of certain virulence factors and an increase in the production of anti-inflammatory molecules, such as IL-10, which was associated with metabolic adaptation.

Conclusion. Metabolic adaptation of S. aureus to the skin environment is driven by metabolic interactions with keratinocytes, leading to changes in metabolic pathways and altered production of virulence factors. These findings suggest that metabolic flexibility and adaptation are key components of S. aureus pathogenesis in atopic dermatitis.

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