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79. Shotgun Metagenomics Reveals Microbial Ecological Features Driving Fecal Microbiota Transplantation Success in Carbapenem-Resistant Enterobacteriaceae Carriers

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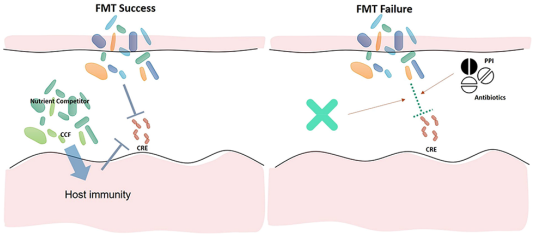
Background. Fecal microbiota transplantation (FMT) is a promising intervention for decolonizing carbapenem-resistant Enterobacteriaceae (CRE); however, predictors of success remain poorly understood. We aimed to identify pre-FMT microbial ecological features, and post-FMT microbiome dynamics associated with FMT efficacy using shotgun metagenomic sequencing.



Methods. FMT was performed in 21 patients colonized with CRE, using stool from 13 rigorously screened healthy donors. Longitudinal stool samples, collected from pre-FMT through 5 weeks post-FMT, underwent shotgun metagenomic sequencing. Patients were classified as responders (n = 9) or non-responders (n = 12) based on CRE clearance. We assessed taxonomic composition (phylum to species level), alpha diversity, dysbiosis scores, and donor–recipient similarity. Clinical metadata, including post-FMT exposure to antibiotics and non-antibiotic drugs (e.g., proton pump inhibitors [PPIs]), were also evaluated.

Results. Responders showed a sustained decrease in CRE abundance along with a marked expansion of Actinomycetota and Bacteroidota. They also demonstrated significant recovery of alpha diversity and reductions in dysbiosis scores with non-responders. Compositional shifts in responders aligned closely with donor profiles, whereas non-responders diverged. This convergence of microbiota in responders was quantified by increasing donor–recipient similarity over time. Pre-FMT microbiota enriched with nutrient competitors, together with post-FMT shifts favoring colonization-permissive taxa (e.g., *Bacteroides* species), correlated with improved outcomes. In contrast, post-FMT exposure to antibiotics and PPIs was associated with decolonization failure at 1 month after FMT.

Conclusion. FMT success in CRE decolonization is facilitated by ecological permissiveness—specifically, the pre-FMT presence of nutrient competitors, along with post-FMT shifts favoring colonization-permissive taxa and with alignment to donor microbiota. These dynamics were modulated by post-FMT exposure to drugs such as antibiotics and PPIs. Our findings suggest that microbiome-informed recipient profiling and rigorous post-FMT antibiotic and PPI stewardship may enhance the efficacy of FMT for CRE decolonization.

Disclosures. All Authors: No reported disclosures