

## Antibiotic-induced gut microbiome and metabolome alterations affects therapeutic FMT efficacy

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### Abstract

Faecal microbiota transplantation (FMT) has become a promising therapeutic approach for treating chronic diseases associated with microbial dysbiosis. However, the impact that taxonomic composition of donor's faecal microbiota has on FMT efficacy is mostly unknown and currently understudied. Here, we investigated how modifications in the donor's microbiota composition affects FMT efficacy and the disease outcome in experimental colitis.

FMT donors were pre-treated with different antibiotics targeting either Gram-positive (vancomycin), Gram-negative bacteria (streptomycin) and strict anaerobes (metronidazole) before administration to colitic mice. The analysis of the gut microbiome, faecal metabolome and the immunophenotyping of colonic lamina propria (LP) immune cells revealed that antibiotic pre-treatment significantly influences the capability of FMT to control intestinal inflammation.

Streptomycin and vancomycin-treated microbiota failed to control intestinal inflammation and were characterized by the blooming of pathobionts previously associated with IBD as well as with metabolites related to the presence of oxidative stress and metabolism of simple sugars. On the contrary, metronidazole-treated donor's microbiota retained its therapeutic efficacy, because of the enrichment of *Lactobacillus*, which has been correlated with innate immune responses involving in particular iNKT cells. By using also a machine-learning approach, we confirmed that FMT is an efficient tool to normalize the gut microbiota during experimental colitis, albeit FMT efficacy is strictly dependent on the microbial community structure of the stool donor.