

Webinar

Precise quantification of bacterial strains after fecal microbiota transplantation explains outcome and candidate strains for Live Biotherapeutics

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Fecal Microbiota Transplantation (FMT), while successful, lacks a quantitative identification of the discrete bacterial strains that stably engraft in recipients, their association with clinical outcomes and a clear roadmap for their use in live biotherapeutics as a safer and scalable alternative to whole stool based FMT.

Using the largest collection of >1,000 unique bacterial strains cultured from a combination of 22 FMT donors and recipients with recurrent *Clostridioides difficile* infection (rCDI), we develop an approach Strainer for detection and tracking of bacterial strains from metagenomic sequencing data. On application to 13 FMT interventions, we detect stable and high engraftment of 71% of microbiota strains in recipients at even 5-years post-transplant, a remarkably durable therapeutic from a single administration. The precise quantification of donor bacterial strain engraftment in recipients independently explained (precision 100%, recall 95%) the clinical outcomes of relapse or success after both initial and repeat-FMT.

We next apply this to the largest successful FMT trial for patients with Ulcerative Colitis (FOCUS study), and found both overall and specific high engraftment of certain bacterial strains and species in patients that achieved the primary endpoint of steroid-free clinical remission with endoscopic remission or response (p value < 0.01). We provide a list of bacterial species and strains that are present in multiple donors and consistently engraft in recipients over time, for use in Live Biotherapeutic Products (LBP) as a safer alternative to FMT.

Our framework can enable the systematic evaluation of different FMT and LBP study designs by quantification of strain engraftment in recipients.

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