IN BRIEF

INFECTION

Bile salt hydrolases involved in the effectiveness of FMT for *Clostridium difficile* infection

A new study published in *Gut* explored the role of bile acid metabolism in the effectiveness of faecal microbiota transplantation (FMT) to treat recurrent *Clostridium difficile* infection (rCDI). Stool samples from patients with rCDI before FMT contained reduced proportions of bacterial species that produce bile salt hydrolases (BSHs) compared with samples collected after FMT. Furthermore, pre-FMT samples contained increased levels of the *C. difficile* germinant taurocholic acid, which negatively correlated with BSH-producing bacterial genera. Following FMT, copy numbers of BSH genes and BSH activity recovered. In vitro studies showed that BSH-mediated hydrolysis of taurocholic acid effectively suppressed *C. difficile* germination. In addition, *C. difficile* viable counts in a mouse model of rCDI were reduced by ~70% after administration of *Escherichia coli* engineered to express highly active BSH.

ORIGINAL ARTICLE Mullish, B. H. et al. Microbial bile salt hydrolases mediate the efficacy of faecal microbiota transplant in the treatment of recurrent *Clostridioides difficile* infection. *Gut* https://doi.org/10.1136/gutjnl-2018-317842 (2019)

GUT MICROBIOTA

Substantial expansion of the human gut microbiota genome catalogue

Multiple studies have analysed the composition of the human gut microbiota using culturing and sequencing methods, but a comprehensive catalogue remains elusive. A new study used 13,133 human gut metagenomic data sets from 75 different studies and reconstructed 92,143 metagenome-assembled genomes from 11,850 human gut microbiomes. Further analysis revealed 1,952 uncultured candidate bacterial species currently absent from high-quality human-specific databases, expanding phylogenetic diversity of the known species repertoire by 281%. The data also improve classification by >200% of less-well-studied samples from Africa and South America. In addition, the new candidate species contain a multitude of new biosynthetic gene clusters and have distinct functional repertoires.

ORIGINAL ARTICLE Almeida, A. et al. A new genomic blueprint of the human gut microbiota. *Nature* https://doi.org/10.1038/s41586-019-0965-1 (2019)

IBD

Autologous adipose tissue injection promising for treatment of perianal fistulas in Crohn's disease

Treatment of perianal fistulas in patients with Crohn's disease with injections of cultured adipose-tissue-derived stem cells is effective but expensive and time-consuming. In a prospective trial in 21 patients with complex perianal fistulas, researchers injected freshly collected autologous adipose tissue instead of stem cells. Additional injections were offered in the absence of complete fistula healing at 6 weeks or at subsequent relapse. After a 6-month follow-up period, fistulas had healed completely in twelve patients (57%), with nine patients requiring one injection, two patients requiring two injections and one patient requiring three injections. Fistulas ceased secretion in three further patients and one patient reported reduced fistula secretion. Short-term proctalgia was the predominant adverse effect.

ORIGINAL ARTICLE Dige, A. et al. Efficacy of injection of freshly collected autologous adipose tissue into perianal fistulas in patients with Crohn's disease. *Gastroenterology* https://doi.org/10.1053/j.gastro.2019.02.005 (2019)

IMMUNOLOGY

Diet modulates T cell-induced colitis via microbial antigen expression

In a study using transgenic mice expressing a T cell receptor (TCR) for specific gut bacteria, researchers have shown how dietary components can affect gut microbiota–host immune interactions, which could lead to new dietary manipulations to manage diseases such as IBD.

In the intestine, gut bacteria elicit $CD4^+$ T cell responses that can be tolerogenic (T_{reg} cell, regulatory T cell) or damage-inducing (T_{eff} cell, effector T cell). These responses are driven by bacteria-specific antigens, and diet is known to modulate bacteria. In the latest study, the investigators sought to determine if certain dietary components affect specific bacterial antigen expression and the subsequent T cell responses.

Prior work showed that colitis could be triggered in a genetically susceptible host by a glycan-degrading member of the gut microbiota, *Bacteroides thetaiotaomicron* (*B. theta*; Bθ). "We wanted to examine the interactions between *B. theta* and host $CD4^+$ T cells in an antigen-specific manner," explains author Paul Allen. "To this end, we generated a TCR transgenic mouse line (BθOM) that expresses a TCR specific for a *B. theta* antigen."

Transfer of T cells expressing the BθOM TCR into healthy mice that had been exposed to *B. theta* led to differentiation of T_{reg} and T_{eff} cells. Colitis was induced when T_{reg} cells were depleted, suggesting that a single *B. theta* protein could drive differentiation of T_{reg} cells that then prevent T_{eff} cell-mediated colitis. "We used this BθOM T cell model to determine how dietary components affect interactions between a

GUT MICROBIOTA

Mendelian randomization reveals causal effects of the gut microbiota

The gut microbiota exerts causal effects on human metabolic traits, according to a new study utilizing Mendelian randomization (MR).

A growing body of evidence supports a role for the gut microbiota in obesity and type 2 diabetes mellitus (T2DM), yet studies to date have been unable to determine causality. Identification of microbiome features causing disease could lead to the development of a new class of microbiota-related therapies. However, the large number of potentially causative features necessitates costly controlled experiments in animals and humans. To circumvent this issue, Serena Sanna and colleagues used MR to assess whether gut microbiota features exert causal effects on metabolic traits in a large human cohort.

MR uses genetic variants known to influence a modifiable exposure as instrumental variables to determine whether that exposure causes disease. "We use genetic differences between individuals that underlie differences in gut microbiome content to connect the microbiome and metabolic disease risk together," explains Sanna. "Because neither the microbiome nor disease can change an individual's DNA sequence, this analysis gives us a much clearer sense of causality."

The researchers assembled genetic data, gut metagenomic sequences, faecal short-chain fatty acid (SCFA) levels and metabolic data for 952 individuals. After identifying microbiome features that correlated with metabolic traits, Sanna and colleagues performed a genome-wide association study to identify loci associated with those microbiome features. Finally, they used MR to