

# Exploiting microbiotic power

Zooming in on gastrointestinal microbiota, a team in Shanghai has developed **SAFE, EVIDENCE-BASED, INNOVATIVE THERAPIES** for digestive disorders and other diseases.

## Trillions of bacteria live in the digestive system.

Known as gut microbiota, they are central to health, influencing conditions ranging from digestive problems and diabetes, to heart disease, cancer and even neurological disorders. Committed to understanding how gut microbiota works, and using this knowledge to prevent and treat diseases, Huanlong Qin, the head of Shanghai Tenth People's Hospital, an affiliate of Tongji University, has led a systematic study of this important system of organisms. His team has also established a microbiota-based treatment regime, and standardized the procedure for faecal microbiota transplant (FMT). Based on the success of his clinical trials, here, Qin discusses the importance of gut microbiota to health, and the clinical benefits of FMT.

## What drove you to focus on gut microbiota?

I started as a surgeon working on gastrointestinal diseases. For patients with severe conditions, we worked on parenteral and enteral nutrition, feeding nutritional products to the body through the veins, or through

a tube into the gut. Thinking about ways to improve gut function, I started working on the role of microbiota. Meanwhile, technological advancement has improved our capabilities to test different bacterial strains and facilitated better understanding of gut microbiota. Around 2014, we began our clinical trials to study the role of gut microbiota systematically.

## How is gut microbiota associated with chronic diseases?

Gut microbiota is like the forgotten organ, because the significance of intestinal health is often overlooked. However, our preliminary investigations have shown that the origin and development of many chronic diseases are closely linked to the structure and richness of gut microbiota. This relationship can be causal, as in the cases of *Clostridium difficile* infection, a bacterial infection of the large intestine, or chronic refractory constipation, where gut microbiota disorder occurs before and potentially leads to these conditions. Sometimes the microbiota disruption may accompany



Huanlong Qin (middle right) and Ning Li (left) co-authored a four-year study on fecal microbiota transplantation

conditions like obesity, diabetes, inflammatory bowel disease (IBD) and colorectal cancer, and deteriorate as the condition progresses. Given this association, gut microbiota should be investigated for potential in intervention strategies for autism and Alzheimer's disease.

## What is your strategy to treat chronic intestinal failure?

Chronic intestinal failure is usually manifested in patients with refractory constipation, severe diarrhoea and IBD, or those who have undergone gastrointestinal surgery as well as radiotherapy and chemotherapy. For them, digestive and absorption dysfunction and long-term intestinal microecological imbalance causes abnormal intestinal motility and bowel movements, causing abdominal distension, and malnutrition, or weight loss. Many of these patients may even show neuropsychiatric symptoms

including depression and phobia. However, there is no effective intervention, and medical knowledge is insufficient.

Our strategy emphasizes improving intestinal microecology, in addition to providing nutrition to the gut. Intestinal microbiota may promote the recovery of chronic intestinal failure by regulating the proliferation of intestinal neural stem cells. We have combined parenteral and enteral nutrition with FMT to regulate intestinal microecology. To maintain the therapeutic effect, microbiota-based intervention alone is sufficient. To date, we have treated around 300 patients using this approach, achieving a success rate of 96%. We have also proposed setting up specialized rehabilitation facilities to standardize the treatment, and have established criteria for diagnosing chronic intestinal dysfunction and evaluating therapeutic effects.

## How did you establish a microbiome-based treatment system?

To make FMT a first-line treatment, we have conducted large-scale clinical trials to evaluate its efficacy and safety. Between 2014 and 2018, we collected clinical data from 2,010 patients with chronic diarrhoea, constipation, IBD and other intestinal disorders, as well as people with autism, and mild intestinal symptoms. Treating them with FMT administered either via nasointestinal tube, capsule, or colonoscopy, we found an overall success rate of 78%, with little adverse effects, proving FMT as a safe and effective treatment. Through the study, we've also standardized the procedure, including rigorous donor selection, microbiome screening and preparation, and evaluation.

The role of gut microbiota goes beyond intestinal diseases. With the standardized system,

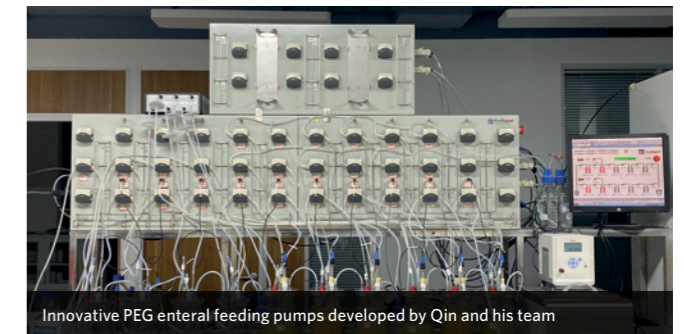
we are now also applying FMT to cancer treatment, as the microbiome also regulates the immune system. When combining FMT with immunotherapy or other targeted therapy for cancer, we also advocate for microbiome metabolic therapy (MMT), surveying metabolites produced by the microbiome.

## What is key for achieving good results from FMT?

Careful selection of donors and recipients, along with rigorous monitoring are vital. In selecting donors, we followed procedures such as those used for organ transplant, screening them for DNA lineage, vaccination history, lifestyle pattern, recent diet and even emotional status, all which affect microbiome conditions. For recipients, we excluded those with severe infections and selected only those showing intestinal symptoms. We carefully monitored patients during the treatment period, to make



FMT capsules for oral use



Innovative PEG enteral feeding pumps developed by Qin and his team

sure standard procedures are followed.

The method of administration also makes a difference. We found using the nasointestinal tube to be more effective than feeding through the colon. We've also developed capsules, adhering to strict industrial manufacturing procedures. As a pioneer for capsule FMT, our hospital is now the largest centre for FMT in the country, having treated the most patients and achieved the best curative effect. Our standardized procedures are easily reproducible, allowing industrial scaling up.

## What are your future plans?

As not everyone is suitable for microbiome transplants, our proposed interventions for now only apply to those with observable intestinal issues. To extend the reach and scope of our research, we are planning a 7,000-square-metre research laboratory with commercial partners, dedicated

to the research of functional microbiomes, targeting the Chinese population.

We are also planning to combine microbiome-based treatment with stem cell therapy to enhance cancer treatment. We are establishing business and academic partnerships to scale up our stool banks to produce enough faecal capsule pills to treat up to 5,000 patients per year. We have started a microbiomics programme using innovative PEG enteral feeding pumps to complete our holistic intestinal health strategies from diagnosis to prevention. All these plans will open research possibilities for our development as a world-leading clinical centre for FMT. ■



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