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Gut microbiota community adaption during young children fecal microbiota transplantation by 16s rDNA sequencing

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ABSTRACT

Fecal microbiota transplantation (FMT) is to restore the intestinal environment of a diseased individual by using of intestinal microbiota from a healthy donor. In recent years, FMT has been developed into a useful treatment method for various chronic gastrointestinal disease. There are already some works attempt to explain the mechanism of this treatment for gastrointestinal diseases in adult patients. However, much less effort has been focused on pediatric gastrointestinal disorders. In this work, we have invited 3 young children with chronic immune-mediated gastrointestinal disorders treated by FMT surgery, and systematically investigated their temporal changes of fecal microbiota after transplantation by 16s rDNA sequencing technology. According to our observations, the fecal microbiota composition of these patients appears obviously interindividual variability and the fecal transplantation significantly increased the species richness in these young patients. The species abundance of *Pasteurellaceae* was remarkably increased during the FMT treatment in all three patients.

1. Introduction

The human gut is colonized by a highly diverse community of microorganisms that play a critical symbiosis with their host, including energy metabolism, immunity and nervous system [1,2]. Studies of the intestinal microbiota imply that an unbalanced microbial community is associated with the pathogenesis of gastrointestinal symptoms. Growing evidence supported that fecal microbiota transplantation could reestablish the balance of gut microbiota community and is an effective treatment against several gastrointestinal symptoms, best known as a treatment for recurrent *Clostridium difficile* infection (CDI) [3], current studies suggested it is also promising results with many other digestive or auto-immune disease, including inflammatory bowel disease (IBD), Irritable Bowel Syndrome (IBS), and Ulcerative Colitis (UC) [4]. It is reported that intestinal gut microbiota appears various bacterial richness and diversity among different diseases [5,6]. The microbiota community studies in CDI indicated that compared with healthy controls, the patients had an initial CDI appears a progressive decrease in species diversity and reduction of *Bacteroidetes* and *Firmicutes* phylum in their fecal samples [3]. A larger cohort study of pediatric Crohn's Disease imply that a set of microorganism taxa associated with disease status, it is might be a bacterial biomarker for early diagnosis [7].

Fecal microbiota transplantation (FMT) is transplantation of a fecal suspension from a healthy donor into the gastrointestinal tract of patient, and to reestablish the balance of intestinal microbiota community of patient. Although FMT has been most accepted treatment for the intestinal microbiota dysbiosis, but the mechanism is still not entirely clear. More research is needed to investigate and understand the dynamic changes of intestinal microbiota community during the FMT treatment, and especially in children patients because children is more impressionable to environmental factors than adult. Gut microbiota studies are commonly performed by analyzing the 16s ribosomal DNA gene (16s rDNA), and it is also current golden standard for microbial community analysis [8,9]. In present study, we applied 16s rDNA sequencing analysis to profile the fecal microbiota community from 3 young children with Juvenile idiopathic arthritis, Ulcerative

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Table 1
Patient information.

Sample	Gender	Age[a]	Sample Info	Disease Info	FMT Info
D01	Female	35 yrs	Donor	Healthy donor	
D03	Female	28 yrs			
R01A	Male	40 m	Patient01	Juvenile idiopathic arthritis	Before FMT
R01C			Donor:D01		1 day after FMT
R01F					1 week after FMT
R01G					2 week after FMT
R02A	Female	19 m	Patient02	Ulcerative colitis (inflammatory bowel disease)	Before FMT
R02C			Donor:D03		1 day after FMT
R02F					1 week after FMT
R02G					2 week after FMT
R07A	Male	37 m	Patient07	Hemophagocytic Syndrome	Before FMT
R07E			Donor:D01		3 day after FMT
R07F					1 week after FMT
R07G					2 week after FMT

[a] yrs: years; m: month.

Table 2
The summary of 16s rDNA sequencing and OTU clustering.

Sample name	Raw data (Mb)	Clean data (Mb)	Number of tags[a]	Number of unique tags	Number of OTU
D01	113.89	53.26	69,717	2324	430
D03	107.24	49.01	70,527	2025	368
R01A	102.26	58.8	71,181	2983	676
R01C	91.88	52.62	69,191	3122	950
R01F	95.22	54.07	69,824	3182	599
R01G	100.22	57.76	70,584	2214	676
R02A	97.28	54.52	68,802	1608	168
R02C	103.55	58.39	71,136	2183	353
R02F	96.33	55.57	70,992	2435	346
R02G	122.13	58.37	70,958	1097	222
R07A	102.58	48.51	69,628	1838	263
R07E	100.19	58.22	71,286	2972	527
R07F	104.17	59.59	68,872	2614	391
R07G	100.4	57.43	69,961	2661	361

[a] The PE reads were assembled to tags according to their paired end relations.

colitis or Hemophagocytic syndrome. The aim of this study was to characterize the changes of microbiota community before and after the FMT for these young children.

2. Material and methods

2.1. Patient information and feces sample process

Three young children (1 female, 2 male; aged 19–40 months) with immune-imbalance related chronic diseases were planning to undergo FMT surgery at Department of Gastroenterology at Shanghai Children's Hospital, and invited to participate in this study. The Shanghai Children's Hospital review board approved this study and we obtained written informed consent for this study from their guardians. Before donating the feces, the two healthy adult donors were screened following test: HIV1/2 antibodies, treponemal antibody, Hepatitis A IgM antibody, Hepatitis B surface antigen, Hepatitis B core antibody and Hepatitis C antibody. The information of patients and donors are listed in Table 1.

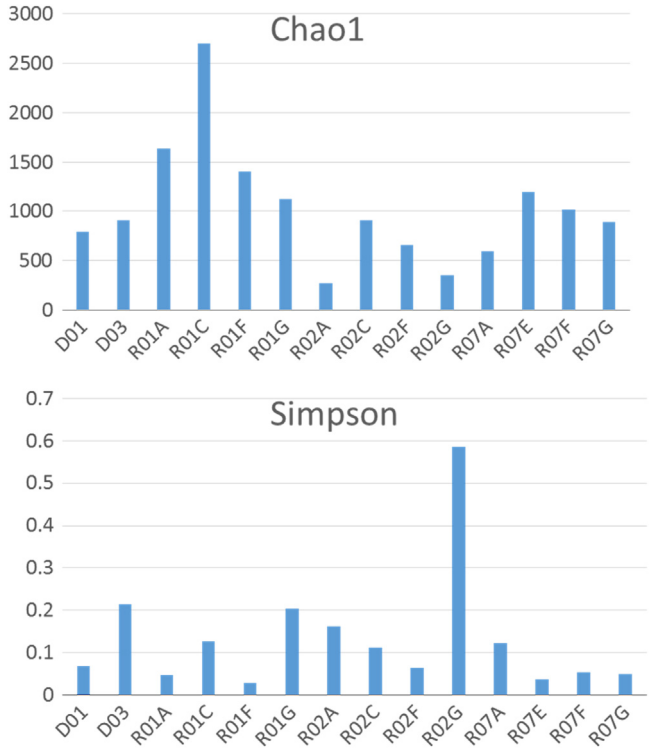

Fig. 1. Alpha diversity of different fecal samples. Up panel is the species richness of microbiota (Chao1 index) and down panel is the species diversity of microbiota (Simpson index). The sample information listed in Table 1.

The collection and analysis of these feces samples were approved by Shanghai Children's Hospital.

The clinical protocol for the allocation of a donor as the feces for FMT was determined by clinic doctors. Feces samples from each donor were collected in standard containers and frozen at −20 °C. The first infusion for FMT surgery was administered into the cecum through nasal jejunal feeding tube. To assess the changes of microbiota community during the FMT treatment, feces samples were collected from the patients at enrollment (before