Ethical issues in human microbiome research

—a case study of fecal microbiota transplantation (FMT)

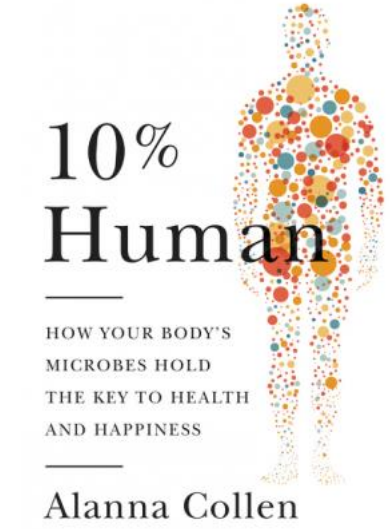
人体微生态研究的伦理问题---以粪菌移植为例

Yonghui Ma
MD. PhD.
yhma@xmu.edu.cn

厦门大学
XIAMEN UNIVERSITY

2017.01.19
@ CUHK Centre for Bioethics

Say hello to your little friends—microbiota

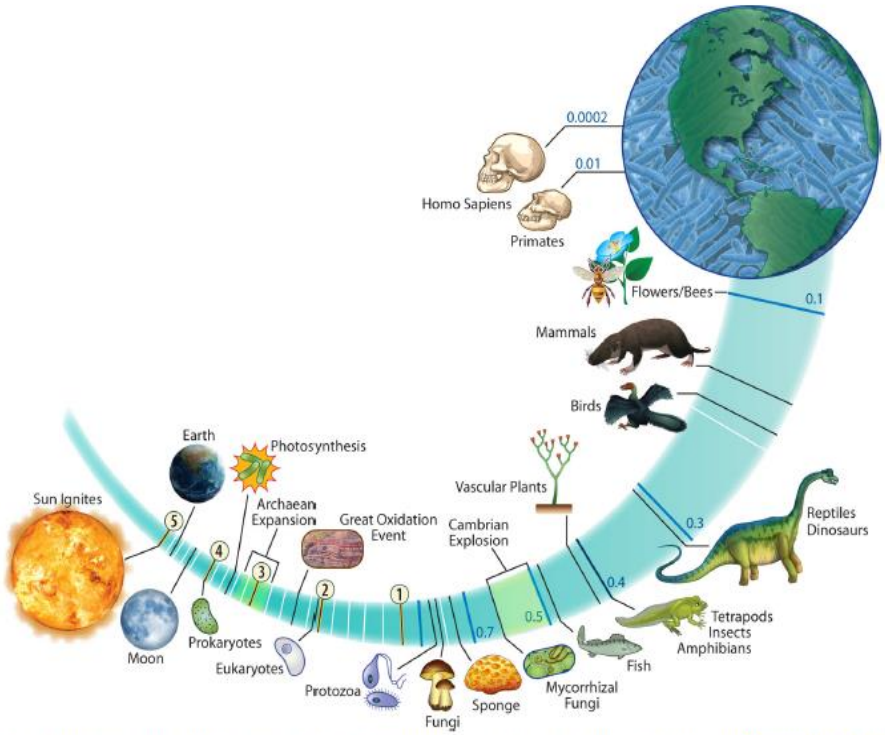


What if someone tell you these:

- You are only 10% human (*Alanna Collen*)
- You are a superorganism (or ecosystem)
- You are your microbes (Jessica Green et al)
- Follow your gut (Rob Knight)
- Being human is a gut feeling *(Thiago Hutter)*

- Your have a second brain in your gut *(Heribert Watzke)*
- Poop(大便）can be medicine /valuable commodity
- ……

Microorganisms have co-evolved with us throughout our evolution



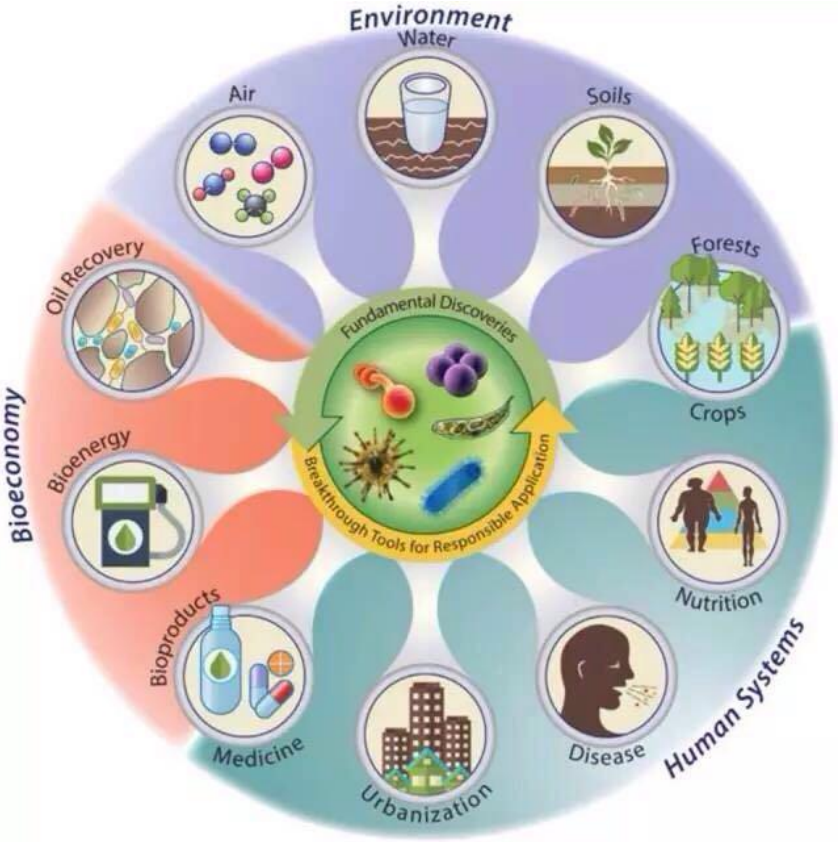
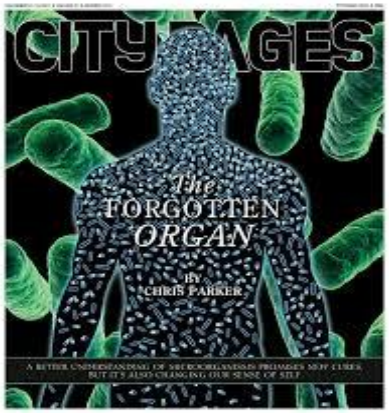


FIG 1 Microbial landmarks in the evolution of our biosphere. Adapted from original artwork of Mariana Ruiz Villarreal (https://commons.wikimedia.org/wiki/File:Timeline_evolution_of_life.svg).

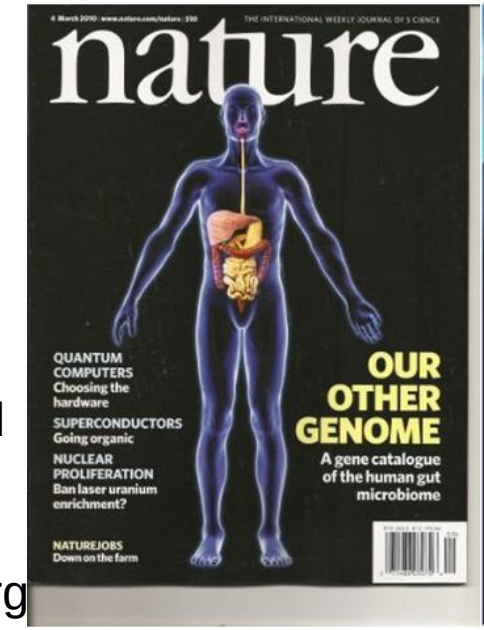
What is gut microbiota? 什么是肠道微生物

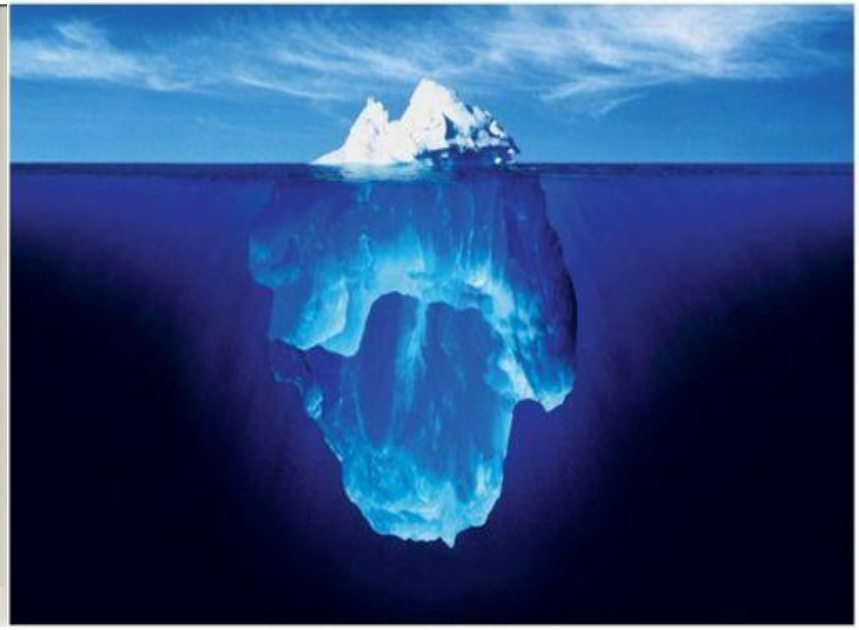
- **Humans are viewed as composites of human and microbial cells**. Human microbiota are complex and dynamic microbial communities composed mainly of bacteria, but also includes protozoa, archaea, viruses, and fungi that resides in and on different body niches such as oral cavity, throat, esophagus, stomach, colon, urogenital tract, respiratory tract, and skin.
- Our gut microbiota contains tens of trillions of bacteria – **10 times** more cells than in our body.
- There are more than 3 millions microbial genes in our gut microbiota –**150 times** more genes than in the human genome.
- Microbiota, in total, can weigh up to **2 kg**.
- The communities in our microbiome carry out **a variety of functions** which are vital to not only our health and well-being but our very survival.
- Exploration of the human microbiome has become a reality due to the availability of powerful metagenomics analysis technologies.



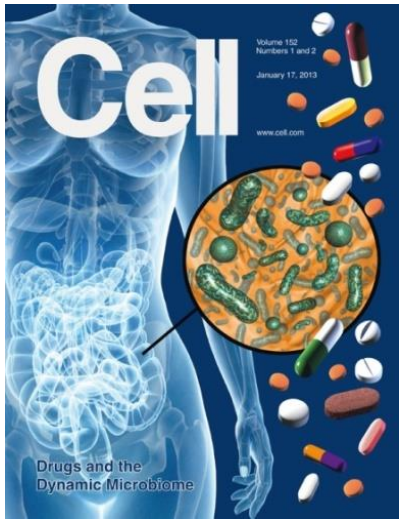
- Forgotten organ
- Virtual organ
- Second brain
- Rainforest
- Our second genome

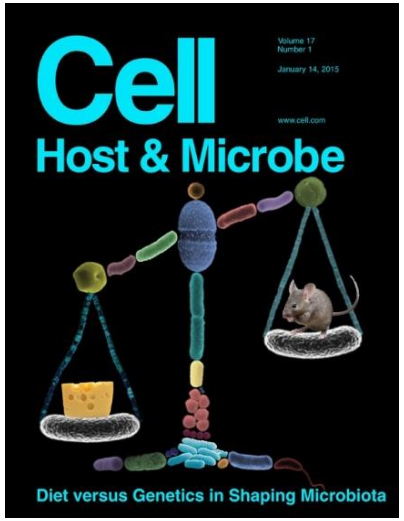
Our understanding and knowledge of human microbiome is still in infancy—a tip of iceberg

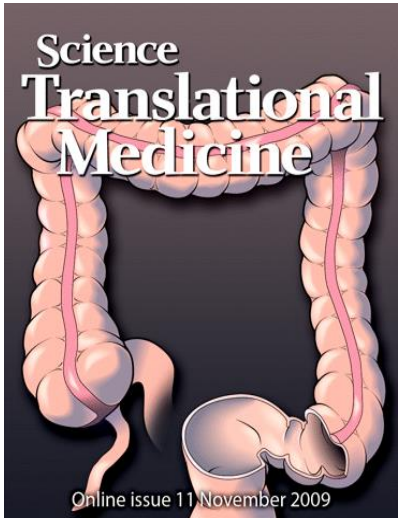


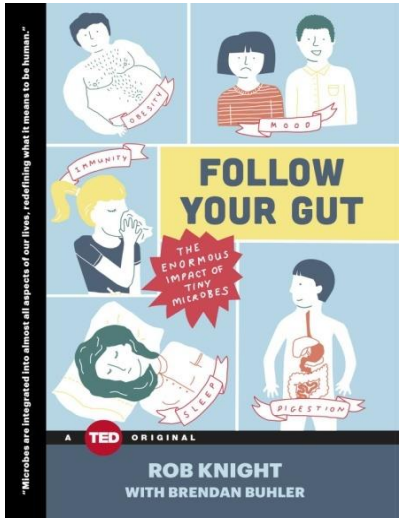


scientific knowledge about microbiome



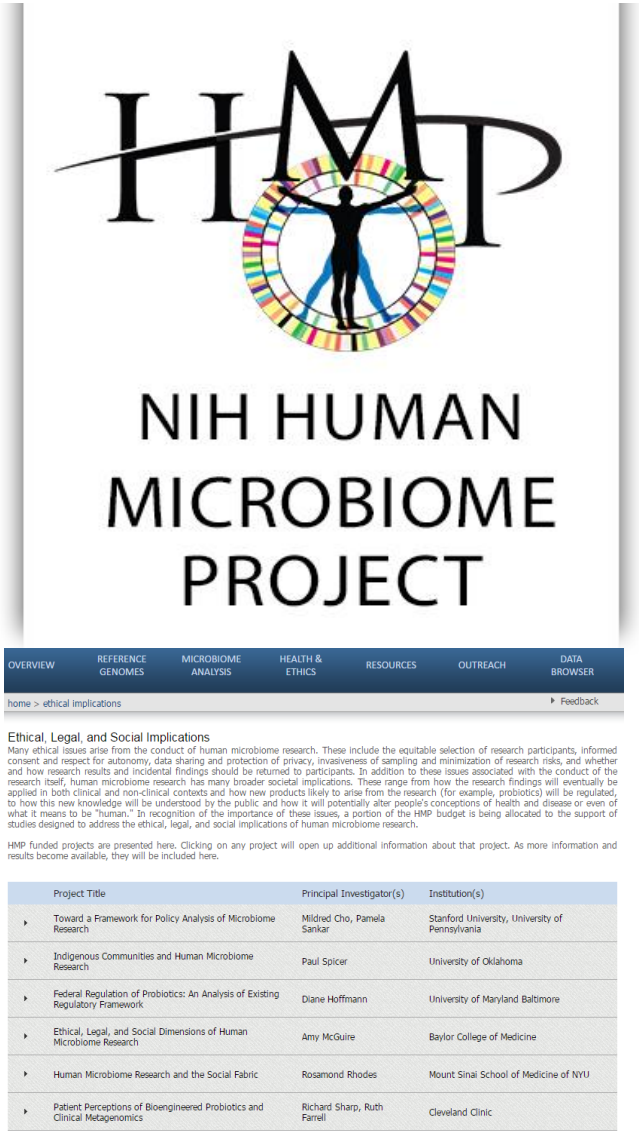






人类微生物组计划（HMP）（2007）

- Development of a reference set of 3,000 isolate microbial genome sequences
- Initial 16S & mWGS metagenomic studies to provide initial answers to the questions of **whether there is a "core" microbiome at each site**
- determine **the relationship between disease and changes in the human microbiome**
- Development of **new tools and technologies for computational analysis,** establishment of a data analysis and coordinating center (DACC), and resource **repositories**
- Examination of the ethical, legal and social implications (ELSI)—led by Prof. Rosamond Rhodes



人类肠道宏基因组计划（MetaHIT）（2007）

MetaHIT is a project financed by the European Commission under the 7th FP program. The consortium gathers 13 partners from academia and industry, a total of 8 countries. Its total cost has been evaluated at more than 21,2 million € and the funding requested from the European Commission has been set with an upper limit of 11,4 million €.

美国国家微生物组计划（May, 2016）

National Microbiome Initiative

Summary:
The new National Microbiome Initiative aims to advance microbiome science in ways that will benefit individuals, communities, and the planet.

Three goals:

- **Supporting interdisciplinary research**
- **Developing platform technologies**
- **Expanding the microbiome workforce**

https://www.whitehouse.gov/blog/2016/05/13/announcing-national-microbiome-initiative

The proposal of Chinese Microbiome Project (Dec1,2016)

香山科學會議

The paradigm shift in treating disease

- Due to the complex symbiotic relationship (共生关系) between gut microbiota and their hosts, alteration of microbial composition can directly disrupt physiologic functions. evidence has been found that associates a number of GI and non-GI diseases with changes in gut microbiota. IBD, Crohn’s, IBS, enteric infections, liver diseases and hepatic encephalopathy (HE). obesity diabetes and other metabolic syndromes, autism, autoimmune disorders and allergies, and some neurological conditions such as Parkinson’s disease.
- Therefore, **it is widely believed that we can improve or prevent some pathological conditions by manipulating the microbiota, instead of, for example, identifying a pathogen and relying on antibiotics to eliminate it.**

Fecal microbiota transplantation is a promising treatment modality

- Among other interventions targeting the intestinal microbiota, the rationale behind Fecal microbiota transplantation has been to introduce a complete, stable community of gut microorganisms to repair or replace the disrupted native microbiota.
- FMT represents a promising and reportedly effective therapeutic alternative for restoring healthy gut microbiota, especially in treating CDI (Clostridium difficile Infection 艰难梭菌感染),
  - **CDI is a severe condition which causes more than 250,000 hospitalizations and kills an estimated 14,000 people in the US each year.**
  - An increasing number of studies have investigated the wider application of FMT, showing it to be effective (to varying degrees) in treating other conditions, such as IBD, IBS, obesity and many others.

Potential of FMT in Treating GI and Non-GI Diseases

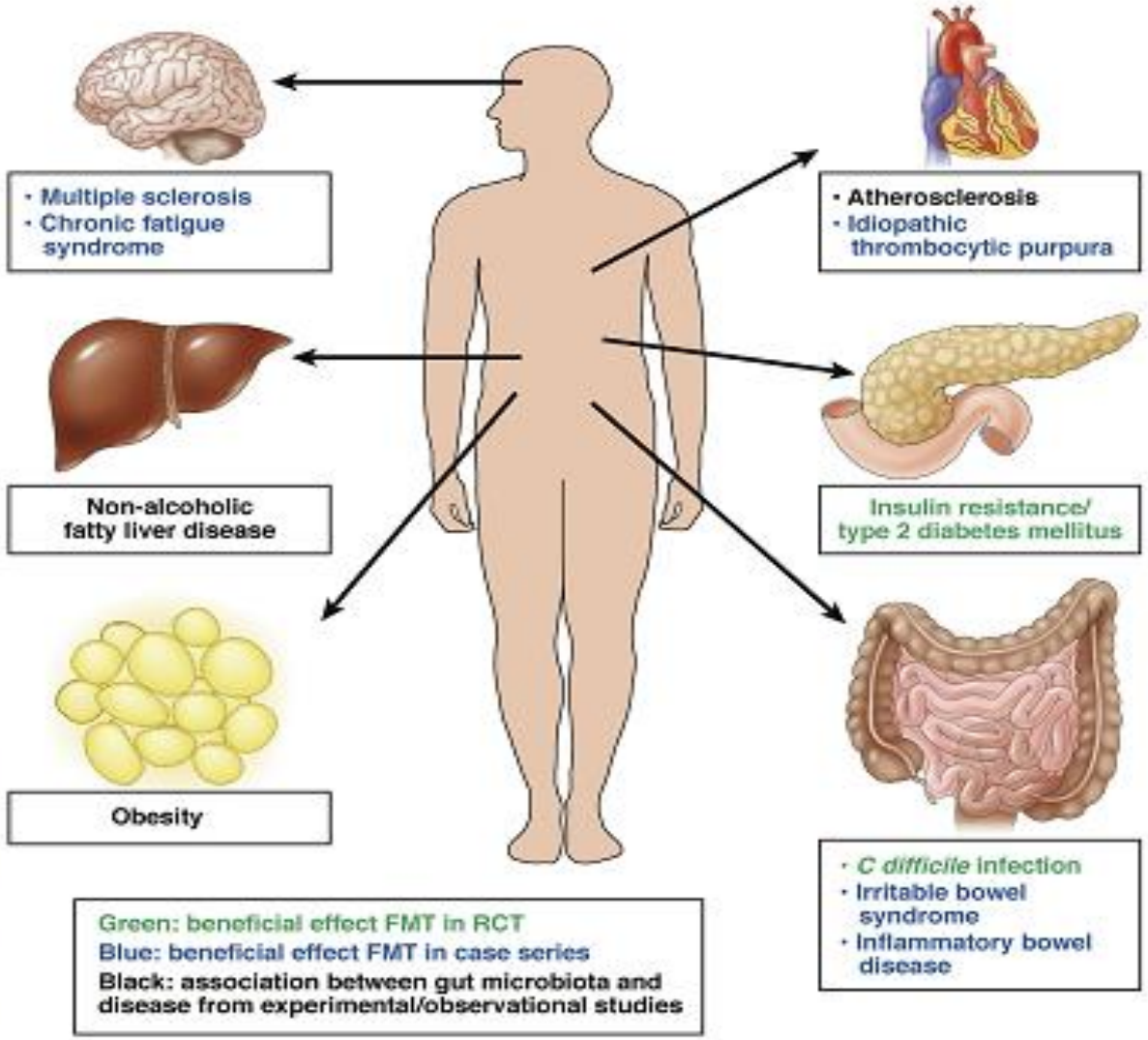


Figure 1. Disorders associated with alterations to the intestinal microbiota that could be treated by FMT. *Green* indicates disorders for which FMT has shown efficacy in randomized controlled trials (RCT), *blue* indicates disorders for which FMT has shown efficacy in case series studies, and *black* indicates disorders that have been associated with disruption of the intestinal microbiota.

A Success Story: FMT

- Fecal Microbiota Transplantation (FMT) refers to infusion of a fecal suspension from a healthy individual (pre-screened) into the GI tract of another person to help to re-establish the functioning microbiota system and cure a specific disease.（via nasogastric tube, upper tract endoscopy, colonscopy, retention enema）

- ✓ **从健康人粪便中获得的功能菌群**
- ✓ **移植到患者肠道内(经鼻饲管、中消化道、肠镜)**
- ✓ **重建肠道新的功能菌群**
- ✓ **治疗肠内外疾病**

Why FMT becomes so popular?

- Rapid effect
- Low cost
- No report of serious adverse effect
- Minimal risk
- Avoid exposure to antibiotics
- Reestablishment of a “balanced” gut microbiota
- Perceived as “natural” and “organic”
- Media coverage portray FMT as “miracle”

Clinical effect of FMT

- Comparison of pre-FMT and post-FMT

A 21-year-old patient with a 10-year history of severe UC, uncontrolled with anti-inflammatory agents, steroids, antibiotics, and finally anti–tumor necrosis factor therapy underwent FMT. Pre-FMT symptoms included severe diarrhea with marked urgency and presence of blood and mucus. The patient underwent colonoscopy where the first FMT was administered. After this, daily rectal infusions were performed for 7 days followed by 26 weekly rectal infusions. The patient experienced an immediate reduction in symptoms, passing 2 formed stools daily without blood, urgency, or mucus. Follow-up colonoscopy at 12 months revealed virtually nil inflammation or edema and she remains clinically well at 12 months on no medication.

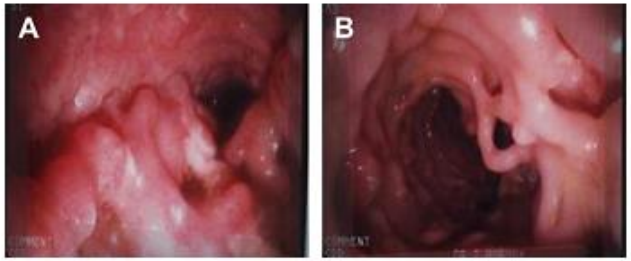


Fig. 1. (*A*) Pre-FMT: edema while on numerous combined therapies. (*B*) Pre-FMT: extensive psueopolyps.

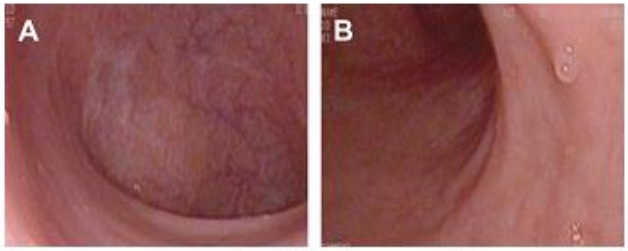


Fig. 2. (*A*) Post-FMT: return to normal, uninflamed mucosa with return of vascular pattern. (*B*) Post-FMT: 1 pseudopolyp in another region.

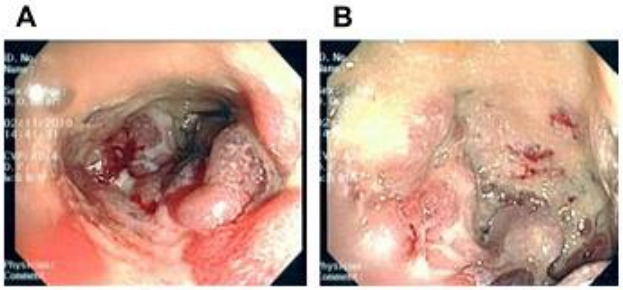


Fig. 3. (*A*) Pre-FMT: severe luminal inflammatory changes initially. (*B*) Post-FMT.

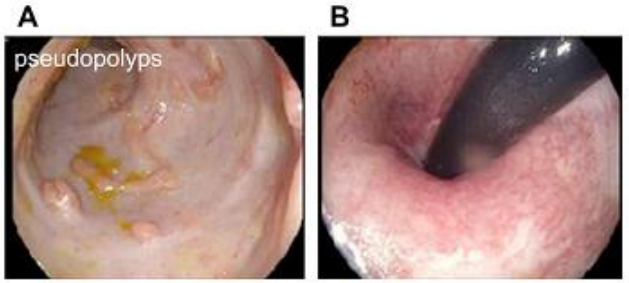


Fig. 4. (*A*) Pre-FMT: some pseudopolyps in the ascending colon at 9 months. (*B*) Post-FMT: healed distal colon showing return of vasculature.

Source: Thomas. Borody, et al. FMT, Techniques, Applications, and Issues. (2012) Gastroenterol Clin N Am

Media coverage and the social enthusiasm

The history of FMT

Table 1
Summary of cases from Eiseman and colleagues

Case	Precipitating Events	Symptoms	Failed Therapies	Response to FMT
Case 1	Gastrectomy. Mixed antibiotic regimen postoperatively.	"Appeared to be in the terminal stages of his critical illness." Abdominal distention, vomiting, bloody diarrhea, marked hypotension.	Vasopressors, hydrocortisone, fluid therapy, albamycin	1 d Post-FMT: marked improvement in condition, bloody diarrhea ceased.
Case 2	Subtotal gastrectomy. Achromycin postooperatively	"Desperately ill" with PMC. Frequent loose, mucoid, greenish bowel movements. On fourth postoperative day—"profound shock appeared moribund."	Hydrocortisone, erythromycin, albamycin, lactobacillus	Diarrhea stopped within 48 h of FMT, "clinical response to fecal enemas was dramatic with disappearance of diarrhea."
Case 3	Preoperative sulfasuxidine and neomycin. Postoperative achromycin, penicillin and streptomycin.	After left hemicolectomy profuse watery diarrhea and fever.		48 h Post-FMT diarrhea completely ceased. Discharged 5 d later.
Case 4	Achromycin for sinusitis	Suddenly developed "severe and life-threatening" profuse watery and bloody diarrhea with fever.	IV fluid and electrolyte replacement. Intramuscular chloromycetin.	Within 24 h diarrhea had ceased. Patient made an "uneventful recovery."

Data from Eiseman B, Silen W, Bascom GS, et al. Fecal enema as an adjunct in the treatment of pseudomembranous enterocolitis. Surgery 1958;44:854–9.

Source: Thomas. Borody, et al. FMT, Techniques, Applications, and Issues. Gastroenterol Clin N Am (2012) 781-803

The history of FMT

【原文】 欲死黄龙汤一升煖以木勺口灌之即活

【厘定】 欲死。黄龙汤① 一升，暖，以木勺口灌② 之，即活。

【校注】

①黄龙汤：即"粪清"。

②灌：据《敦煌古医籍考释》当为"灌"。

【按语】 黄龙汤，《大明本草》："（主治）天行热狂热疾、中毒、蠱毒、恶疮"。而朱震亨谓之"（主治）热毒湿毒、大解五脏实热"。《本草纲目》卷五十二引《肘后备急方》治野葛芋毒、山中毒蕈"欲死者。并饮粪汁一升，即活"。与本方相类。

《肘后备急方》（handbook of prescription for emergency）--葛洪

Should We Standardize the 1,700-Year-Old Fecal Microbiota Transplantation?

Faming Zhang, MD, PhD[1],
Wensheng Luo, MSc[2], Yan Shi, CMD[1],
Zhining Fan, MD[1] and Guozhong Ji, MD[1]

This letter underwent AJG editorial review.

doi:10.1038/ajg.2012.251

To the Editor: We reviewed the multicenter long-term follow-up study using the fecal microbiota transplantation (FMT) for recurrent *Clostridium difficile* infection by Brandt group (1). The study demonstrated efficacy with 91% primary cure rate and

This was reported in the first Chinese handbook of emergency medicine, "Zhou Hou Bei Ji Fang" (or "Handy Therapy for Emergencies"), which also first described treatment of *Plasmodium falciparum* malaria by *Artemisia annua* containing artemisinin (4). To our knowledge, this book should therefore be considered the first literary record of application of fecal transplantation through the mouth or upper gastrointestinal tract. Later, in the Ming dynasty of the 16th century, Li Shizhen described a series of prescriptions using fermented fecal solution, fresh fecal suspension, dry feces, or infant feces for effective treatment of abdominal diseases with severe diarrhea, fever, pain, vomiting, and constipation in the most-known book of traditional Chinese medicine, "Ben Cao Gang Mu" (Compendium of Materia Medica). For aesthetic considerations, the herb doctors

The rationale of FMT

- The idea behind FMT includes the re-introduction of a complete, stable community of gut microorganisms aimed at repairing or replacing the disrupted native microbiota to correct the underlying imbalance.
- It is presumed this microbiota repair eradicates or hinders pathogens, which maybe causing the targeted condition (e.g. Clostridium difficile Infection,CDI)

Indication and application of FMT

TABLE 1. Disorders associated with an altered intestinal microbiome

GI
Cholelithiasis
Colorectal cancer
Hepatic encephalopathy
Idiopathic constipation*
IBS*
IBD*
Familial Mediterranean fever
Gastric carcinoma and lymphoma
Recurrent *Clostridium difficile* infection*
Non-GI
Arthritis
Asthma
Atopy
Autism*
Autoimmune disorders
Chronic fatigue syndrome*
Diabetes mellitus and insulin resistance*
Eczema
Fatty liver
Fibromyalgia*
Hay fever
Hypercholesterolemia
Idiopathic thrombocytopenic purpura*
Ischemic heart disease
Metabolic syndrome*
Mood disorders
Multiple sclerosis*
Myoclonus dystonia*
Obesity
Oxalic acid kidney stones
Parkinson's disease*

IBS, Irritable bowel syndrome; *IBD*, inflammatory bowel disease.
*Some reports on improvement or cure with fecal microbiota transplantation.

Source: Lawrence J. Brandt. Etal. An overview of fecal microbiota transplantation: techniques, indications, and outcomes. 2013 Gastrointestinal Endoscopy

Methodology of FMT

- FMT comprises the administration f a fecal solution from a donor into the intestinal tract of a recipient.
- A standardised protocol rooted in evidence-based practice is still lacking.
  - FMT donor screening protocols
    - FMT Working Group (Bakken et al. 2011)
    - Current Consensus Guidance on Donor Screening and Stool testing for FMT (Relman et al. 2013)
    - Amsterdam Protocol (Smits et al. 2013)
- It’s already been proposed that some adverse effect and even failure are related to the variables in methodology from different medical institutions, not the concept of FMT.

Methodology of FMT (cont.)

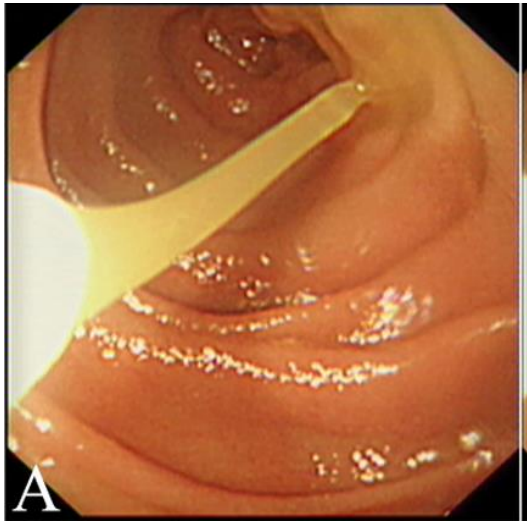
Donor selection
- Family members or friends
- Rigorous screening of pathogens and infections

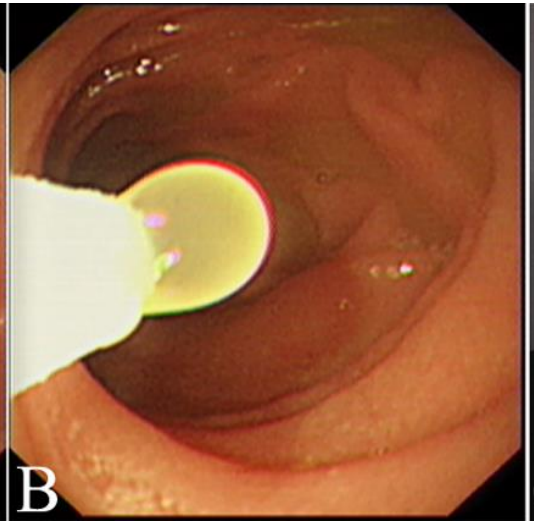
Preparation of FMT **material**
- Varying studies on preparation of material
- Diluents: Water and normal saline both reported

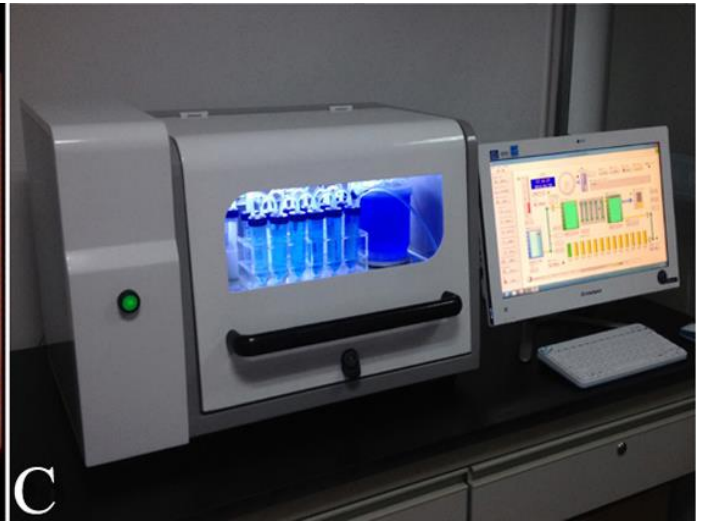
Routes of **administration**
- Infused by various methods, nasogastric tube, upper tract endoscopy, colonscopy, retention enema
- The best route depends on the location of the disease

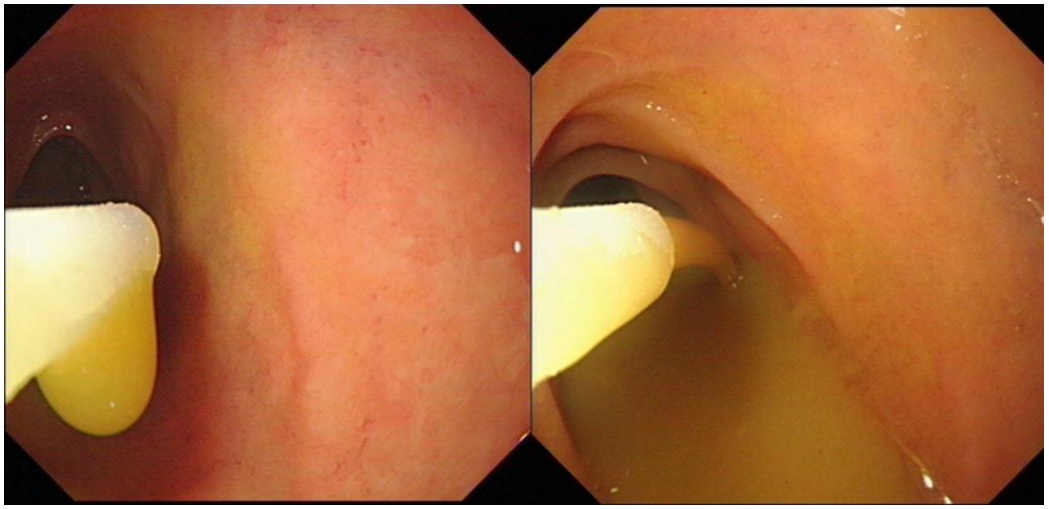
Adverse **events**
- No serious adverse events
- Diarrhea, rare abdominal cramping or constipation, fever
- Insufficient long-term follow up data

内镜下简易质控方法









简易质控

放大内镜下液滴不见颗粒
镜头入液不可见异色杂质
喷洒到壁上不可见颗粒
颜色为乳黄或者淡黄
正确理解颜色

Cui et al. ICS. 2015. **Research highlight**

Methodology of FMT (cont.)

Source: picture taken during field study at Medical Center for Digestive Diseases, the Second Affiliated Hospital of Nanjing Medical University, Nanjing, China.

Characteristics of FMT—innovation intervention

- FMT is still an unproven and exploratory treatment, its therapeutic mechanisms is still unknown.
- Our understanding about the composition and types of gut microbiome community is very limited
- It is unknown what strategies should be employed to prepare the patient for transplantation
- It is unknown what quantity and type of organisms should be used, and how the treatment might be delivered
- Shortgun approach: there is a large discrepancy between the low-key technology used in this treatment and the sophisticated knowledge of the intestinal microbiome.

Social, ethical, and legal issues of FMT

Ethical issues surrounding FMT

1. Self and personal identity
2. Informed consent and vulnerability of patients
3. Risk and safety about FMT
4. Privacy and confidentiality
5. Commercialisation of FMT

1. Conceptual and philosophical implications (cont.)

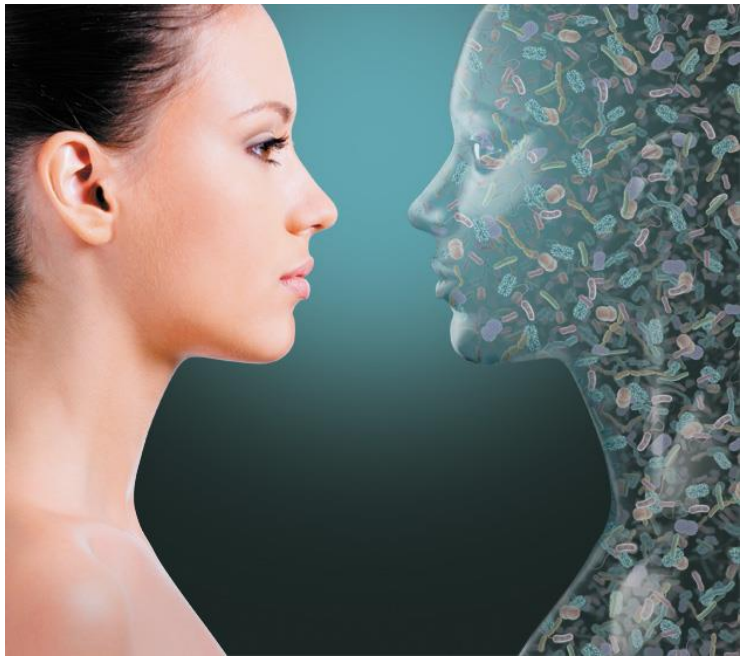
- Human microbiome research will alter the concept and perception of health and disease
  - What kind of microbiome profile can be considered as healthy?
  - How to determine a "suitable healthy donor"? No agreed conceptual definition. Two dimensions:
    - The ideal (optimal) donor: we don't know what constitutes an "optimal" microbiota profile
    - The healthy donor: clinical suitability, blood tests, stool screening, interview including medical history, physical examinations.
    - Uncertainties associated with donor profile: age limits, children? Pregnant? Nursing women? Religious background?

Conceptual and philosophical implications (cont.)

- Human microbiota exist in and on every human body and play key role in our daily life.
  - **the dichotomy of human VS non-human and self VS non-self collapse**. are “they" part of us or part of the environment?
  - Our attitudes and perception towards bacteria need to be changed. In the past, we launched the war on bacteria—who are we really harming? Hand-wash and some hygiene practices (absence of microbiome can cause illness!)

Conceptual and philosophical implications (cont.)

Married to our gut microbiota?



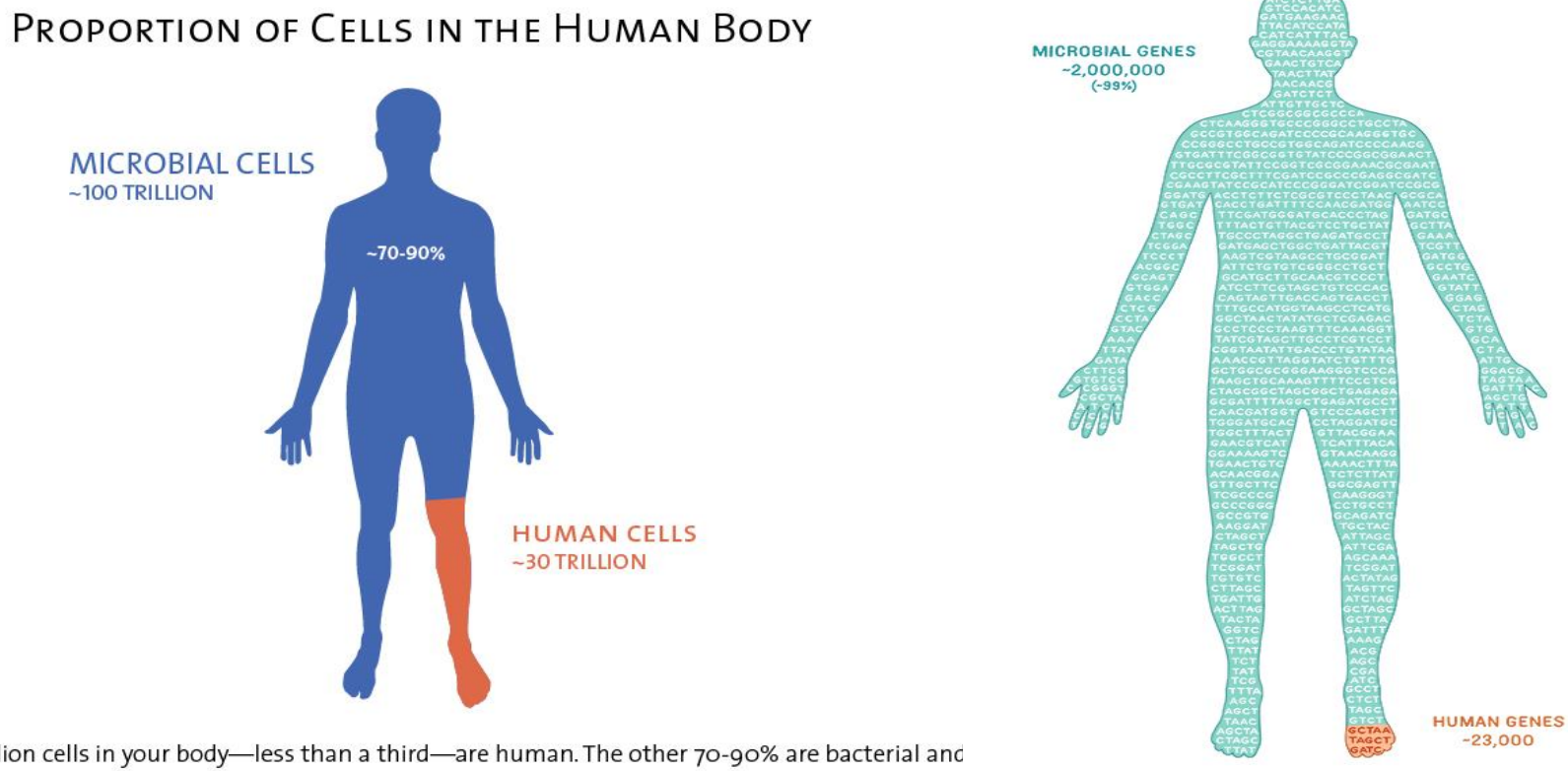
“Are we more microbe than man?”

Should we be tailoring treatment to both our human and microbial ‘selves’?

---Katrina Ray, Nature Reviews Gastroenterology October 2012

Conceptual and philosophical implications

"Are we more microbe than man?"
"How they defend and define us" (by Carl Zimmer, *New York Times*)
"our Microbiomes, ourselves" (by Carl Zimmer, *New York Times*)
"Human as superorganism comprised of the human body and the collection of microbes that inhabit the human body." (Rosamond Rhodes)



2. Informed consent and patient vulnerability

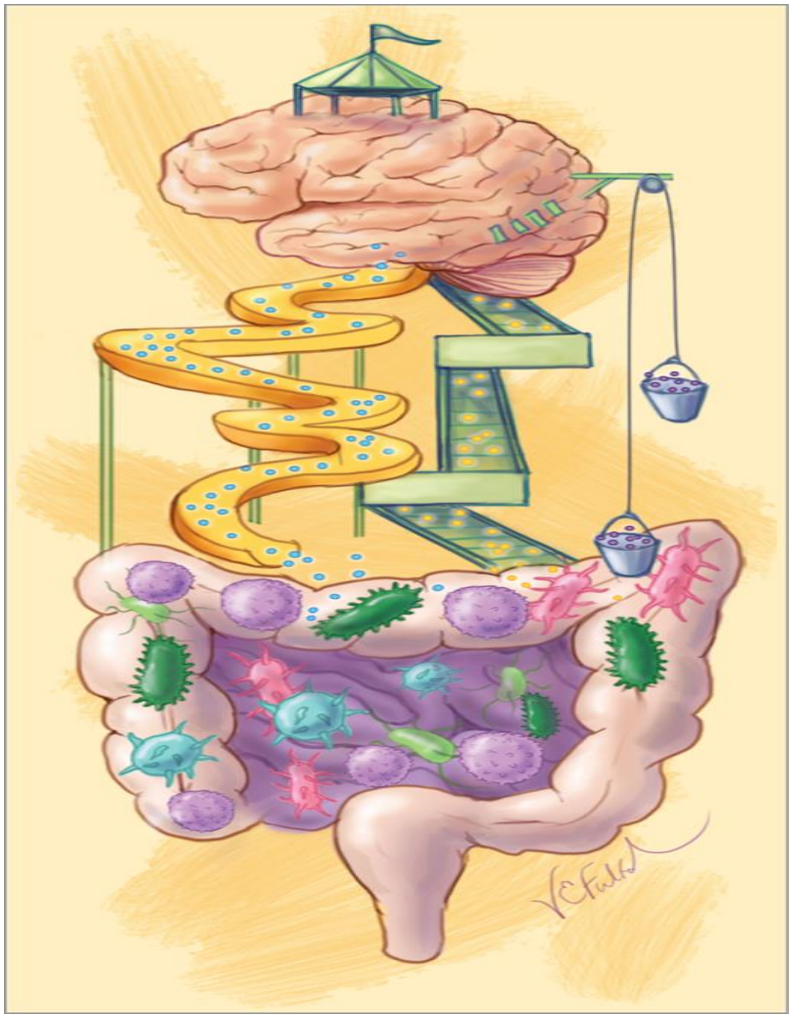
- based on our limited knowledge about the human microbiome, it is challenging to identify and explain the potential risks and benefits of participating in human microbiome research or accepting FMT treatment/trials.
- FMT candidate patients(e.g. IBD)' autonomy may be compromised by their stress and desperation, affecting their ability to give informed consent.
- Their capacity to be informed may also be affected by a diminished ability to appropriately process information about risk. Both aspects may make them susceptible to deception or inducement.
  - Failure of other medical therapies
  - potential effective therapy and "last straw"

3. Risks and safety about FMT

- Current research suggests FMT is safe and no serious adverse events have been reported, but there many areas in which evidence is lacking and further investigation is needed.
- FMT: **“natural”” organic” and “safer”??**
  - Clinical risk: transmission of pathogens, transfer of multiple viral lineages 医学风险：感染
  - Social and legal risk: “**microbial fingerprints(微生物指纹)**”, privacy breaches 社会和法律风险：隐私暴露
  - Mental and psychological risk: emotions, behaviour, personality alterations? potential transmission of anxiety and depression? 精神和心理风险：焦虑和抑郁的传播？行为改变？

3. Risks and safety(cont.)

- Interactive relationship between gut microbiota and the central nervous system in regulating moods and behavior, influencing brain function and behavior.
  - microbial transplant research in mice models which show gut microbiota influencing stress and anxiety-related behaviors
  - germ-free mice with "depression microbiota" derived from human patients with Major Depressive Disorder (MDD) resulted in depression-like behaviors
  - These studies raise the question of whether FMT might alter the neurological state of recipients



Picture source: M.J.Friedrich. JAMA. 2015

Risks and safety (cont.)

- whether and how to extend screening programs in order to mitigate these risks
- **Three questions arise**
  - **First,** whether FMT donors should be screened not only for pathogens but for a history of psychiatric and psychological illness, e.g. mood disorders?
  - **Second,** by manipulating the gut microbiota, FMT could be used as a way to affect the brain and consequently "sculpting behaviour".
  - **Third,** by transferring mood/mind-altering microbes, FMT carries the possibility of altering a person's personality and identity (positively and negatively).
- our current characterization of FMT as "natural" and "organic" and therefore "safer" may be **premature and naive.**

4. Privacy and Confidentiality (cont.)

- “personal microbiomes contain enough distinguishing features to identify an individual over time”. microbial DNA may contain even more information about a person than their human DNA.
- **Microbial fingerprints**: unique to individual (mobile phone screen, pet), identification—increased scope for forensic investigation? Or by law enforcement or homeland security agencies?
  - firstly, stool contains human DNA that is identifiable to particular individuals;
  - secondly, fecal microbiota could be indicative of past behavior. For example, bacteria unique to a particular locale, if found in a person’s feces, may reveal that they have travelled to that region, and this may be of interest to homeland security agencies.

Case Study: Our unique Microbial Fingerprints

BBC Sign in | News | Sport | Weather | Shop | Earth

NEWS

Home | Video | World | Asia | UK | Business | Tech | Science | Magazine

Health

Mobile phones carry owners' bacterial 'fingerprint'

By Helen Briggs
Health editor, BBC News website

24 June 2014 | Health

BIOTECHNOLOGY

In Forensics, Microbiome May Become Next Fingerprint

MAY 12, 2015 09:40 AM ET // BY AFP

DNEWSvideo

Explainer: The President Sepp

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH
Powerful ideas for a healthier world

A to Z Index | Search | GO

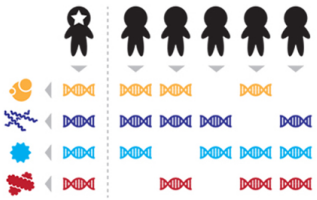
People • Calendar • myHarvardChan • Email • Newsletters

News

- News Home
- Press Releases
- Features
- Multimedia
- In the News
- HPH Magazine
- Alumni Stories
- Faculty Stories
- Student Stories
- Explore Research by Topic
- The Kiosk: E-News and Notices
- Office of Communications
- Make a Gift

Home > News > Press Releases > Personal microbiomes shown to contain unique 'fingerprints'

Personal microbiomes shown to contain unique 'fingerprints'



Taken together, DNA sequences from four microbial species distinguish the starred person's ...biome from the microbiomes of five other people

Explore research by topic

SEARCH PRESS RELEASE ARCHIVES

Search

FEATURES

Global health
Women's contribution to health care nearly 5% of global GDP

Privacy, Confidentiality, and discrimination

Discrimination and stigmatisation surrounding mental illness and neurological disorders

- Concerns: microbiome research data may be prematurely or incorrectly interpreted regarding e.g. susceptibility to mental or metabolic disorders, or the ethnic background of the patient.
- physicians and scientists need to exercise caution when handling and interpreting this information, especially in forensic investigation.

5. Commercialisation of FMT

- Property rights: can fecal microbiota profiles be patented? "optimal microbiota profile" or a "disease-targeted fecal microbiota profile"? How should we think about ownership and property rights relating to various aspects of FMT?
- Potential commoditisation of FMT: cash or kind?
- Direct-to-consumer of FMT: internet posting, "do-it-yourself" home protocols
  - forgoing standard medical care and the guidance of certified healthcare professionals, patients put their safety at risk.
  - provide an opportunity to exploit patients rather than empowering them
  - give consumers the false impression that a quick fix can undo poor lifestyle decisions

FMT related Biobank

Challenge: physicians do not have consistent, easy access to healthy stool.

- FMT stool Bank
  - Provide frozen preparations of screened and filtered human stool for use in FMT therapies.
  - Research use
- Human Microbiome Research Bank
  - **OpenBiome and AdvancingBio in the USA,**
  - **the Taymount Clinic in the UK,**
  - **the Netherlands Donor Feces Bank (NDFB),**
  - **the Chinese FMT bank.**
  - **…**

Microbiome companies

SERES THERAPEUTICS™

中华粪菌库
fmtBank.org

μBiome Clinical

Rebiotix
Microbiota Restoration Therapy

MicroBiome therapeutics

锐翌基因
REALGENE

SECOND GENOME
THE MICROBIOME COMPANY

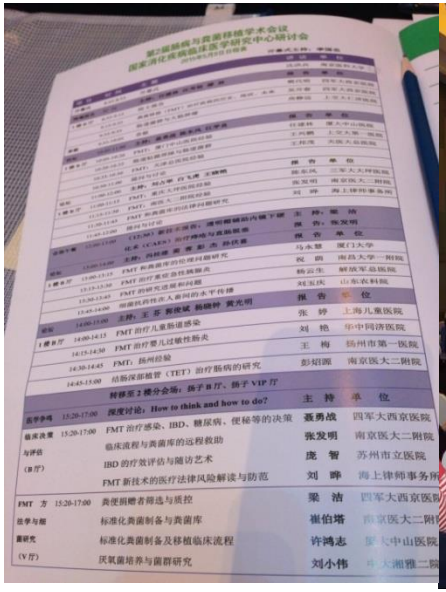
FMT and public health

- FMT also has ethical and social implications for public health.
  - FMT is officially indicated for cases of recurrent CDI in which antibiotic treatment has failed. This means that antibiotic use could be avoided if FMT were used as an earlier intervention.
  - Infection control programs need to be reframed to capitalise on the expanding understanding of the protective role of the microbiome
  - Given shared nature of human gut microbiome across families and communities (transferred through birth modes, diet, lifestyles), modulating an individual's gut microbiome may have unknown health consequences for their family.
  - "obligation to our common microbial environment and the stewardship of the shared microbiome" (O'Doherty et al, 2016)

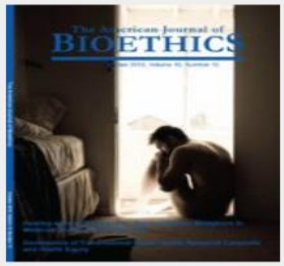
Conclusion

- FMT has the potential to be an **innovative, low-tech, and inexpensive approach** to effectively treating a variety of diseases.
- The social, ethical, and legal implications of FMT therapy, however, are **complex and worthy of careful consideration** by healthcare professionals and regulatory bodies.
- Patient desperation is not the reason to provide this treatment. **Safety and the protection** of vulnerable patients should be primary consideration.
- **More clinical trials** are necessary to study the potential of FMT for treatment of disorders other than CDI.
- We have to **proceed with caution** in any such microbial intervention involving the introduction (or removal) of bacteria, especially when we don’ t know the long-term impacts of combinations of interacting microbiome.

Some of my academic activities regarding FMT



Some publications related to FMT



The American Journal of BIOETHICS

Vol. 16 No. 10 | October 2016

ISBN: 1526-5161

Yonghui Ma, et al, Ethical issues in Fecal Microbiota Transplantation in practice. American journal of bioethics, 2017 (in press) , SCI & SSCI,IF 6.5

中华消化杂志

马永慧, 等. 粪菌移植的伦理、社会问题探讨 [J]. 中华消化杂志, 2016,36(12): 861-863. DOI:10.3760/cma.j.issn.0254-1432.2016.12.019

BioMed Central

BMC Medical Ethics

Yonghui Ma, et al, How physicians face ethical and social challenges in fecal microbiota transplantation: a questionnaire study (accepted), BMC Medical Ethics, 2017

References (selected)

- Faming Zhang, et.al Should we standardize the 1,700-year-old Fecal Microbiota Transplantation? (2012) AJG.
- Katrina Ray, Married to our gut microbiota . (2012) Nature Reviews.
- Lawrence J. Brandt. Etal. An overview of fecal microbiota transplantation: techniques, indications, and outcomes. (2013) Gastrointestinal Endoscopy.
- David T. Rubin etal. Curbing our Euthusiasm for Fecal Transplantation in Ulcerative Colitis. (2013) AJG.
- Alice K Hawkins, et al. "Who owns your poop?" : insights regarding the intersection of human microbiome research and the ELSI aspects of biobanking and related studies. (2011) BMC Medical Genomics
- Amy L. McGuire et al. Ethical, legal, and social considerations in conducing the Human Microbiome Project. (2008) Genome Research
- Thomas. Borody, et al. FMT, Techniques, Applications, and Issues. (2012) Gastroenterol Clin N Am.
- Thomas J. Borody et al. FMT: indications, methods, evidence, and future directions. (2013) Curr Gastroenterol Rep.
- Loek P.Smits Et al. Therapeutic Potential of FMT. (2013) Gastroenterology.
- Kelly CR,Mellow M, Stollman N. 2014. FDA's role in regulating FMT is imperative burdensome. *American Gastroenterological Association Pespectives* 9: 6-9.
- Smith MB, Kelly C, Alm EJ. 2014. How to regulate faecal transplants. *Nature* 506:290-291.
- Rhodes R, Gligorov N, Schwab A (eds.) 2013. The Human Microbiome: Ethical, Legal and Social Concerns. Oxford University Press.

It’s time we cultivate a friendship with our microbiome!

Email: yhma@xmu.edu.cn

In dreams, poop is actually a symbol of money.

---Sigmund Freud

Xiamen（厦门）welcome you!