The Basics and what the gastroenterologist needs to know

- Definitions
- Microbiome techniques
- GI diseases with dysbiosis
- Targeted treatments designed to change gut microbiome
- Future targets
Basic Definitions: What is the human Microbiome?

- Microbe: tiny living organism living in an established environment, i.e. bacterium, fungus, protozoan, or virus
- Microbiome AKA “Superorganism”: collectively all the microbes in the human body and their genome capacity in the human gut
- <30% of gut microbiome has been cultured
- Flora refers to plants only
- Composed of approximately $10^{14}$ bacterial cells
- This is 10 x more than cells in the body

Gut microbiome

Seven phyla constitute most of the gut microbiome:

- Firmicutes, Bacteroidetes, Proteobacteria, Fusobacteria, Verrucomicrobia, Cyanobacteria and Actinobacteria.
- Firmicutes and Bacteroidetes make up 90% of gut microbiota.
- Make up 1 kg of adult body weight
- Dysbiosis: A disturbance in the microbiota community
- Commensal: organism that lives in intimate contact with another and derives benefit without harming or benefitting the other.
- Symbiont: Benefits from the other
- Pathobiont: Possibly pathologic organism which under normal circumstances lives as a symbiont
- Large scale surveys of gut microbiome
  - Human Microbiome Project in USA
  - MetaHIT in Europe


Biofilms

- a community of microbes that live together on a surface
- A vast number of the pathogens in our body are in communities called biofilms
- Bacteria form an extracellular matrix around the colony that protects them from antibiotics
- Within the matrix, they communicate using quorum sensing
- **Quorum sensing** is the regulation of gene expression in response to fluctuations in cell-population density.
- Biofilms are analogous to multi-cellular organisms
Pre, Pro and Syn-Biotics

- **Prebiotics:** Non-digestible polysaccharides that stimulate growth of digestive bacteria
  - Examples: Lactulose or inulin
  - On ingestion they stimulate growth of beneficial bacteria already present in the host and promotes health of the host
  - Usually increase concentrations of Bifidobacterium spp.
- **Probiotics:** Live microorganisms that reconstitute the gut microflora
- **Synbiotic:** combination of prebiotic and probiotic
  - Very few studies using both.


Microbiome analysis techniques

Majority of techniques for microbiome analysis are now based on DNA extraction and amplification of 16S ribosomal RNA (rRNA) genes.
- DNA fingerprinting: DGGE, RISA, TRFLP, DNA microarrays, FISH, qPCR
- These rRNA genes are conserved between bacterial species and vary in a way allowing their ID.
- **Metagenomics:** Study of collective genomes from the environment
- **Metabome:** Collective array of metabolites present in a biological sample

Fraher & Quigley et al., Nrgastro 2012.
### Techniques used to characterize gut microbiota

<table>
<thead>
<tr>
<th>Technique</th>
<th>Description</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture (prior to 1990s)</td>
<td>Bacterial isolation</td>
<td>Cheap</td>
<td>Labor intensive &lt;30% cultured</td>
</tr>
<tr>
<td>qPCR</td>
<td>16S RNA amplification and quantification</td>
<td>Quantitative, fast, phylogenetic identification</td>
<td>PCR bias, can't identify unknown species</td>
</tr>
<tr>
<td>DGGE/TGGE</td>
<td>Gel separation of 16S rRNA</td>
<td>Fast, semi-quantitative</td>
<td>PCR bias, no ID of phylogenese</td>
</tr>
<tr>
<td>T-RFLP</td>
<td>Digested fragments separated by gel electrophoresis</td>
<td>Fast, cheap and semi-quantitative</td>
<td>Low resolution, PCR bias and no ID of phylogenoses</td>
</tr>
<tr>
<td>FISH</td>
<td>Fluorescently labeled hybridization of target 16S rRNA sequences</td>
<td>Phylogenetic ID, Semi-quantitative</td>
<td>Needs probe sequences, cannot ID unknown species</td>
</tr>
<tr>
<td>DNA microarrays</td>
<td>Fluorescence detected w/ a laser</td>
<td>Phylogenetic ID, fast and semi-quantitative</td>
<td>Cross hybridization, PCR bias, low level species difficult</td>
</tr>
<tr>
<td>Cloned 16S rRNA gene sequencing</td>
<td>Cloning of full-length 16S rRNA</td>
<td>Phylogenetic ID, quantitative</td>
<td>PCR bias, laborious, expensive, cloning bias</td>
</tr>
<tr>
<td>Direct sequencing of 16S rRNA amplicons</td>
<td>Massive parallel sequencing of partial 16S rRNA amplicons</td>
<td>Phylogenetic ID, fast and unknown bacteria can be ID Quantitative</td>
<td>PCR bias, expensive, laborious</td>
</tr>
<tr>
<td>Microbiome shotgun sequencing</td>
<td>Massive sequencing of whole genome</td>
<td>Phylogenetic ID, quantitative</td>
<td>Expensive, computationally intense data gathering</td>
</tr>
</tbody>
</table>

Adapted from Fraher et al. NRGastro 2012

### Which technique to use?

- **DGGE**: First-pass rapid assessment of gut microbial composition analysis
- **qPCR**: is great for high-profile total bacterial load
- **FISH**: total bacterial load analysis for specific phyla or species
- **Shotgun sequencing**: Small samples with phylogenetic ID and quantitative analysis

Adapted from Fraher et al. NRGastro 2012
Consequences of intestinal infection in the developing and developed worlds

- Developed world
  - Functional GI disorders
  - Reactive arthritis
  - Celiac disease
  - Inflammatory bowel disease

- Developing world
  - Environmental enteropathy
  - Tropical sprue
  - Malnutrition
  - Cognitive impairment
  - Growth stunting
  - Vaccine hyporesponsiveness

Adapted from Riddle and Walker et al. Am J Gastroenterology Suppl 2016; 3: 1-3

Strong association of infectious gastroenteritis with IBS:
The Epidemiology of Irritable Bowel Syndrome in the US Military:
Findings from the Millennium Cohort Study

<table>
<thead>
<tr>
<th>Hazard ratios</th>
<th>Any IGE</th>
<th>Medical encounter IGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antecedent IGE</td>
<td>Any IBS (95% CI)</td>
<td>Highly probable IBS (95% CI)</td>
</tr>
<tr>
<td>None</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>2.10 (1.15-3.87)</td>
</tr>
<tr>
<td>Female</td>
<td>3.04 (1.31-6.90)</td>
<td>2.94 (1.53-5.69)</td>
</tr>
<tr>
<td>Service branch</td>
<td>Army</td>
<td>2.06 (1.06-4.03)</td>
</tr>
<tr>
<td>Navy/Crest Guard</td>
<td>0.95 (0.59-1.52)</td>
<td>Ref</td>
</tr>
<tr>
<td>Marine Corps</td>
<td>0.93 (0.51-1.73)</td>
<td>Ref</td>
</tr>
<tr>
<td>Air Force</td>
<td>1.85 (0.41-8.78)</td>
<td>Ref</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>No light</td>
<td>Ref</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.61 (0.33-1.12)</td>
<td>Ref</td>
</tr>
<tr>
<td>Heavy</td>
<td>0.92 (0.49-1.74)</td>
<td>Ref</td>
</tr>
<tr>
<td>BMI</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Normal/underweight</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Overweight</td>
<td>0.77 (0.61-0.99)</td>
<td>Ref</td>
</tr>
<tr>
<td>Obese</td>
<td>0.62 (0.46-0.87)</td>
<td>Ref</td>
</tr>
</tbody>
</table>

Disturbance in gut bacteria leads to disease

- Gastrointestinal disorders
  - (IBS, IBD, NASH)
- Obesity
- Diabetes
- Sjogrens
- Cancer
  - (gastric, esophageal, colon)
- Heart Disease
- Autism?, MS
- Allergies and asthma

Strategies to modify gut microbiota

- Less invasive or safer
- FMT
  - Gut-Directed Antibiotics
- Prebiotics
  - Systematic exclusion diets
  - Stopping PPIs
- Probiotics
  - FODMAP diet

Adapted from Simrén et al. Gut 2013; 62: 159-176.
Positive and negative effects of microbiota on gut barrier structure and function

R. Gnavus and R. torques
Mucin degraders

Bifidobacterium spp. & Lactobacillus spp
produce antiinflammatory metabolites

Streptococcus spp. or Staph Aureus cause an immune response

Pathogenesis of IBS: Microbiota and their influences

Function of gut bacteria:

- Bile acid deconjugation effecting stool volume and consistency
- Fermentation (gas production)
- Modulation of communication with the brain
- Immune activation
Dysbiosis in IBS

- Fecal DNA PCR sequencings of 16S rRNA data shows dysbiosis of bacteria in IBS

- IBS-D have higher levels of Enterobacteriaceae (P=0.03) and lower Fecalibacterium (P=0.04) in general than non-IBS (HC)
Gut microbiota composition in African children from rural areas versus Italian city children: could diet be a factor?

Crosstalk of the immune system with gut microbial and the environment in IBD
Baharak Moshiree, MD, MS-CI

Alterations in gut microbiome and cancer

- Gastric cancer: *Helicobacter pylori*
  - Elevated antibody titers against cagA have higher risk of gastric adenocarcinoma

- Esophageal cancer
  - *H. pylori* may be protective by inhibiting parietal cell function and/or inducing development of atrophic gastritis
  - Loss of *H. pylori* may alter gastric microflora and result in reflux-mediated esophageal cancer

- Colon cancer
  - “CASUALTY THEORY” of Sears and Garret- Cell Host Microbe. 2014; 35: 327-328.
  - microbiota are either primary (initiators) or secondary (promote progression) contributors
  - Procarcinogenic traits: *Fusobacterium, Streptococcus gallolyticus* (*S. bovis*) and adherent-invasive *E. coli*


FODMAPS Influence gut transit and the microbiome

- Osmotic effects
- Luminal pH
- SCFA (butyrate, propionate, acetate)
- Trophic effects
- Microbiome changes
- Increased biomass
- GI symptoms (pain, gas/bloating, altered bowel movements)
- Acceleration of transit time
- Bacterial fermentation
- Gas production (CH₄, H₂, CO₂)
- Effects on
  - Motility
  - Visceral sensation
  - Immune activation
  - Permeability

Cognitive and emotional factors

US Data: Low FODMAP Diet (LFD) versus mNICE for IBS-D patients

N=45 low FODMAP (LFD), 39 mNICE
No difference in composite endpoints (P=0.13)
Composite endpoints:
Primary: The proportion of patients reporting adequate relief of IBS-D symptoms ≥25% of intervention weeks 3–4.
Secondary: composite end point which required response in both abdominal pain and stool consistency.

Compared with baseline scores, the low FODMAP diet led to greater reductions in average daily scores of abdominal pain, bloating, consistency, frequency, and urgency than the mNICE diet.

Is LFD all good?

- LFD compared with Sham diet (n=95)
  - First placebo controlled study w FODMAP diet.

- LFD resulted in lower IBS-SSS score as c/w Sham (P=0.001) and lower stool acetate

- Lower abundance of Bifidobacteria and less microbial diversity was seen with LFD

- Probiotics resulted in higher stool abundance of Bifidobacteria but did not effect the IBS-SSS or HRQOL
FODMAPS alter metabolites, increase microbial richness and decrease histamine levels in IBS

Pros of LFD:

Urine histamine levels decreased with LFD and IBS-SSS was reduced in LFD (p=.001) after 3 weeks intervention (n=20 in each group)

After 3 weeks intervention, LFD group had higher Actinobacteria diversity (P=.02)

HFD had more Ruminococcaceae (5.5%) accounting for variability in symptoms between two groups.

HFD decreased relative abundance of bacteria involved in gas consumption.

Cons:

No difference in diversity within or between community between BL and after diet

Porphyromonas species increased also after the LFD (P=0.01) and bifidobacteriaceae increased with HFD (p=0.063)

McIntosh K et al. Gut 2016; 0: 1-11

Proposed Beneficial effects of probiotics

- Acceleration of colonic transit
- Reduction of bloating
- Reversal of intestinal muscle function
- Improve inflammation beyond the mucosa
- Decrease immune-related activation of enteric motor and sensory neurons.
- Alter bile acid metabolism thru deconjugation (alter motility and secretion)
- Reduction of bacterial fermentation
- Alter stool gas and volume

Meta-analysis of probiotics for IBS

- 43 RCTs total. 19 RCTs higher quality (n=1650 IBS patients)
- Probiotics improved global IBS symptoms, abdominal pain, bloating and flatulence score
- Individual species of combination effects were marginal
- More modest benefits with high quality studies (RR=0.86, CI 0.72-1.03) versus low quality (RR=0.52, CI 0.35-0.77)
- RR of IBS symptoms persisting with probiotics vs placebo was 0.79 (95% CI 0.70-0.89)
- Published literature over-represents small studies
- NNT=7 (95% CI 4-12.5)
- NNH=35
Recommendations for probiotic use in IBS/IBD and Infectious Diarrhea: 2015 consensus update

<table>
<thead>
<tr>
<th>Clinical Condition</th>
<th>Effectiveness</th>
<th>Specific Strain of Organism and Strain References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>A</td>
<td>A. Lactobacillus casei, Leuconostoc mesenteroides</td>
</tr>
<tr>
<td>Infectious childhood—intoxication</td>
<td>B</td>
<td>B. L. acidophilus, Bifidobacterium breve</td>
</tr>
<tr>
<td>Prevention of infection</td>
<td>C</td>
<td>C. L. rhamnosus, B. lactis</td>
</tr>
<tr>
<td>Prevention of AAD</td>
<td>D</td>
<td>D. L. helveticus, B. bifidum</td>
</tr>
<tr>
<td>Prevention of recurrent C. difficile</td>
<td>E</td>
<td>E. L. casei, L. rhamnosus</td>
</tr>
<tr>
<td>Prevention of CDAD</td>
<td>F</td>
<td>F. L. casei, L. rhamnosus</td>
</tr>
<tr>
<td>IBD</td>
<td>G</td>
<td>G. L. casei, L. rhamnosus</td>
</tr>
<tr>
<td>Proctitis</td>
<td>H</td>
<td>H. L. casei, L. rhamnosus</td>
</tr>
<tr>
<td>Prevention and maintaining remission</td>
<td>I</td>
<td>I. L. casei, L. rhamnosus</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>J</td>
<td>J. L. casei, L. rhamnosus</td>
</tr>
<tr>
<td>Inducing colitis</td>
<td>K</td>
<td>K. L. casei, L. rhamnosus</td>
</tr>
<tr>
<td>Maintenance</td>
<td>L</td>
<td>L. L. casei, L. rhamnosus</td>
</tr>
<tr>
<td>Crohn’s</td>
<td>M</td>
<td>M. L. casei, L. rhamnosus</td>
</tr>
<tr>
<td>IBS</td>
<td>N</td>
<td>N. L. casei, L. rhamnosus</td>
</tr>
</tbody>
</table>


4th Triennial Yale/Harvard Workshop on Probiotic Recommendations.

Evidence for Gut-microbiota-brain communication: Probiotics affect central processing of emotion and sensation in healthy women

Fermented milk product with probiotic (FMPP) (n=12) bid X 4 weeks compared with no intervention (n=13)

Components: Bifidobacterium animalis subsp Lactis, Streptococcus thermophiles, Lactobacillus bulgaricus, and Lactococcus lactis subsp Lactis

Brain regions showing reduced activity in response to an emotional faces attention task after FMPP intervention are shown, with significant regions demarcated.

Tillisch et al. Gastroenterology. 2013 Jun;144(7):1394-401
Antibiotics (Rifaximin) alter the natural history of IBS up to 10 weeks (range 6-24 weeks)

Outcomes at 4 Weeks

<table>
<thead>
<tr>
<th>Adequate Relief of Global IBS Symptoms</th>
<th>Adequate Relief of IBS-Related Bloating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients, %</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>TARGET 1</td>
<td>TARGET 2</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>P=0.01</td>
<td>P=0.03</td>
</tr>
<tr>
<td>40.8</td>
<td>31.2</td>
</tr>
<tr>
<td>(n=306; n=314)</td>
<td>(n=315; n=330)</td>
</tr>
</tbody>
</table>


Fecal Microbiota Transplantation

- Stool from a healthy individual is instilled into a sick person to cure a disease
- Purpose: reconstitute the normal microbial homeostasis and break the cycle of antibiotic agents disrupting the microbiome
- Lower GI delivery is better
- Indications:
  - Moderate CDI not responding to standard therapy for at least a week
  - Recurrent CDI: 3 or more episodes of mild to moderate CDI and failure of vancomycin taper, or
  - 2 episodes of CDI resulting in hospitalization

Resolution rate
- 90% overall
  - lower: 91%
  - upper: 82%
- No AEs

Kassam et al. Am J Gastroenterol, 2013

FMT for patients with recalcitrant CDI

Resolution of symptoms:
1. Healthy intestine
2. Healthy microbiota
3. Healthy colon
4. Healthy immune system

Resolution of symptoms:
1. Healthy intestine
2. Healthy microbiota
3. Healthy colon
4. Healthy immune system

Hospital-related infections: *Clostridium difficile* is NUMBER ONE

1978 - First case of reported *C. difficile* infection
- Pseudomembranous colitis was a known entity related to antibiotic use
1984 – commercial availability of ELISA testing
2000-2008 – hypervirulent strain emerged

Risk factors: Host factors such as age, comorbid illnesses, immunosuppression, *altered microbiome* (antibiotics, PPI, GI procedures)
- Hospitalization (ICU stay)

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>All Health Care-Associated Infections (N = 100)</th>
<th>Pneumonia (N = 50)</th>
<th>Surgical Site Infections (N = 100)</th>
<th>GI Infections (N = 50)</th>
<th>UTIs (N = 50)</th>
<th>Bloodstream Infections (N = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td><em>Clostridium difficile</em></td>
<td>61 (22.1)</td>
<td>1 (2.0)</td>
<td>60 (24.0)</td>
<td>1 (2.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>54 (10.7)</td>
<td>18 (36.0)</td>
<td>17 (35.0)</td>
<td>1 (2.0)</td>
<td>2 (3.0)</td>
<td>7 (14.0)</td>
</tr>
<tr>
<td><em>Klebsiella pneumonia</em></td>
<td>50 (9.9)</td>
<td>13 (26.0)</td>
<td>13 (26.0)</td>
<td>1 (2.0)</td>
<td>17 (25.0)</td>
<td>4 (8.0)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>47 (9.3)</td>
<td>3 (6.3)</td>
<td>14 (28.0)</td>
<td>1 (2.0)</td>
<td>18 (27.0)</td>
<td>5 (10.0)</td>
</tr>
<tr>
<td><em>Enterococcus species</em></td>
<td>44 (8.8)</td>
<td>2 (3.5)</td>
<td>16 (32.0)</td>
<td>5 (10.0)</td>
<td>11 (19.0)</td>
<td>6 (12.0)</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>36 (7.3)</td>
<td>14 (25.0)</td>
<td>7 (14.0)</td>
<td>1 (2.0)</td>
<td>10 (17.0)</td>
<td>2 (4.0)</td>
</tr>
<tr>
<td><em>Candida species</em></td>
<td>32 (6.4)</td>
<td>4 (8.0)</td>
<td>3 (6.0)</td>
<td>3 (6.0)</td>
<td>3 (6.0)</td>
<td>11 (22.0)</td>
</tr>
<tr>
<td><em>Streptococcus species</em></td>
<td>25 (5.0)</td>
<td>8 (16.0)</td>
<td>8 (16.0)</td>
<td>2 (4.0)</td>
<td>2 (3.0)</td>
<td>2 (4.0)</td>
</tr>
<tr>
<td><em>Clostridium difficile</em>-negative <em>Staphylococcus species</em></td>
<td>24 (4.8)</td>
<td>9 (18.0)</td>
<td>7 (14.0)</td>
<td>0</td>
<td>1 (1.5)</td>
<td>9 (18.0)</td>
</tr>
</tbody>
</table>
Dysbiosis $\rightarrow$ Harmony

**PRE-FMT**
- microbial diversity and richness
- urobilinogen
- fecal tryptic activity
- all fatty acids
- microbial function (metabolome)
- INCREASE in Proteobacteria

**POST-FMT**
- Firmicutes and Bacteroidetes
- butyrate-producing organisms
- secondary bile acids
- DECREASE in Proteobacteria

---

Fecal Microbiome in Recurrent *C. difficile* (R-CDI) is less diverse

Patients with R-CDI had decreased phylogenetic richness

**Bacteroidetes** and **Firmicutes** are reduced in patients with R-CDI not in patients with just one episode of CDI

---

C. diff treatments

Traditional antibiotics
- Metronidazole
- Vancomycin
- Fidaxomicin

Biological therapies
- FMT
- Spore therapy
- Non-toxigenic c difficile

Immune-based therapies
- Antibodies against toxin A/B
- IVIG/Oral IgG

Risks of FMT and potential ethical concerns

<table>
<thead>
<tr>
<th>Observed</th>
<th>Potential</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal discomfort</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>Bloating</td>
<td>HIV</td>
</tr>
<tr>
<td>Acute infections (bacterial, viral and parasitic)</td>
<td>Autoimmune diseases</td>
</tr>
<tr>
<td>Acute allergic reactions</td>
<td>Obesity</td>
</tr>
<tr>
<td>Flare of ulcerative colitis</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td></td>
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<tr>
<td>Worse diarrhea</td>
<td></td>
</tr>
<tr>
<td>Increased CrP</td>
<td></td>
</tr>
<tr>
<td>Orthostasis</td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td></td>
</tr>
</tbody>
</table>

Could we also predispose the recipient to the diseases that donor will develop in future?

<table>
<thead>
<tr>
<th>Disease or Condition</th>
<th>Proposed Mechanism</th>
<th>Evidence</th>
<th>Possible Therapies for altering microbiota</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDI</td>
<td>Reduced microbial diversity</td>
<td>Animal and human studies</td>
<td>FMT for recurrent CDI</td>
</tr>
<tr>
<td>IBS</td>
<td>Reduced microbial diversity and decreased Bacteroidetes</td>
<td>Animal and human studies</td>
<td>Probiotics, non-systemic antibiotics (rifaximin), FMT trials starting</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Reduced microbial diversity</td>
<td>Human studies</td>
<td>Probiotics (VSL#3) for pouchitis, FMT trials ongoing</td>
</tr>
<tr>
<td>Obesity and metabolic derangements</td>
<td>Reversed Firmicutes to Bacteroides ratio</td>
<td>Animal and Human studies</td>
<td>Trials of FMT ongoing</td>
</tr>
<tr>
<td>Allergic disorders</td>
<td>Reduced microbial diversity</td>
<td>Animal and human studies</td>
<td>Studies of probiotics ongoing, not for FMT</td>
</tr>
<tr>
<td>Neuropsychiatric illness</td>
<td>Disrupted intestinal barrier</td>
<td>Human studies</td>
<td>None for FMT</td>
</tr>
</tbody>
</table>


Diversity breeds good health

Learning from our Bugs

Learning to Love Our Bugs
The countless microorganisms that live inside us are more important than we realized as symbiotic partners in health

By Jerry Grillo, Illustrations by Gula Opine

Jerry Grillo. Emory Medicine. Fall 2016 Edition