

What's new in gut microbiota research?

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Royal City Men's Club

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Presenter disclosure

- **I am co-founder and CSO of NuBiyota LLC,** a company focused on commercializing Microbial Ecosystem Therapeutics, which I will mention in this forum



Human health depends on microbiota health



Bacteria,
yeasts,
archaea,
viruses,
protists

We are super-organisms of human and microbial cells
We exist in a delicate host : microbe equilibrium

How human *are* we?

- 'Reference human'
 - 70 kilograms, 20–30 years old, 1.7 metres tall
- ~30 trillion human cells
- 39 trillion bacterial cells

Human **1 : 1.3** Bacteria

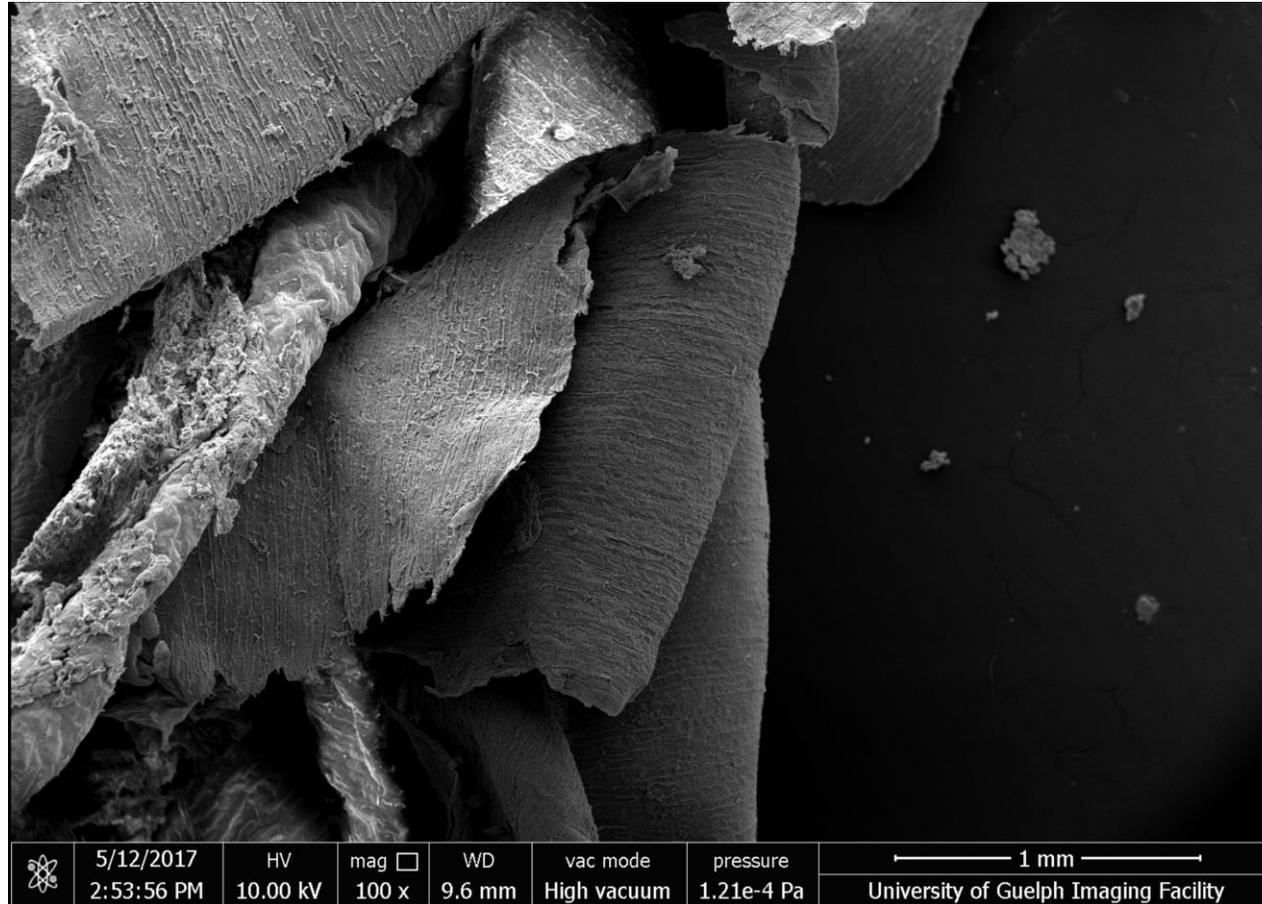
But then, why don't we look like bacteria?

- Bacterial cells are much, much smaller than human cells
 - On average 1/100 to 1/1000 of the size
 - Each gram of feces contains $\sim 10^{11}$ bacterial cells

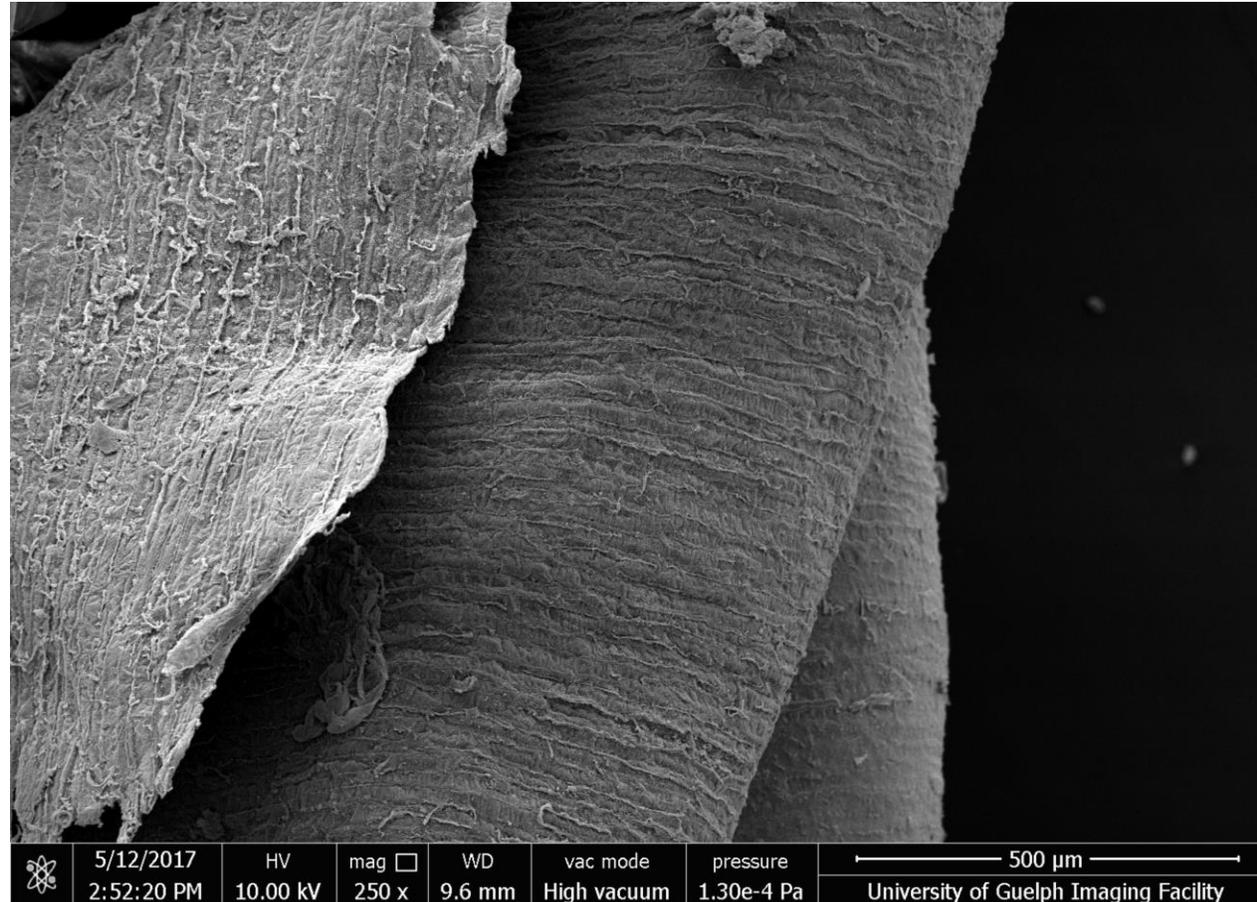


That's 10 trillion cells in the average bowel movement!

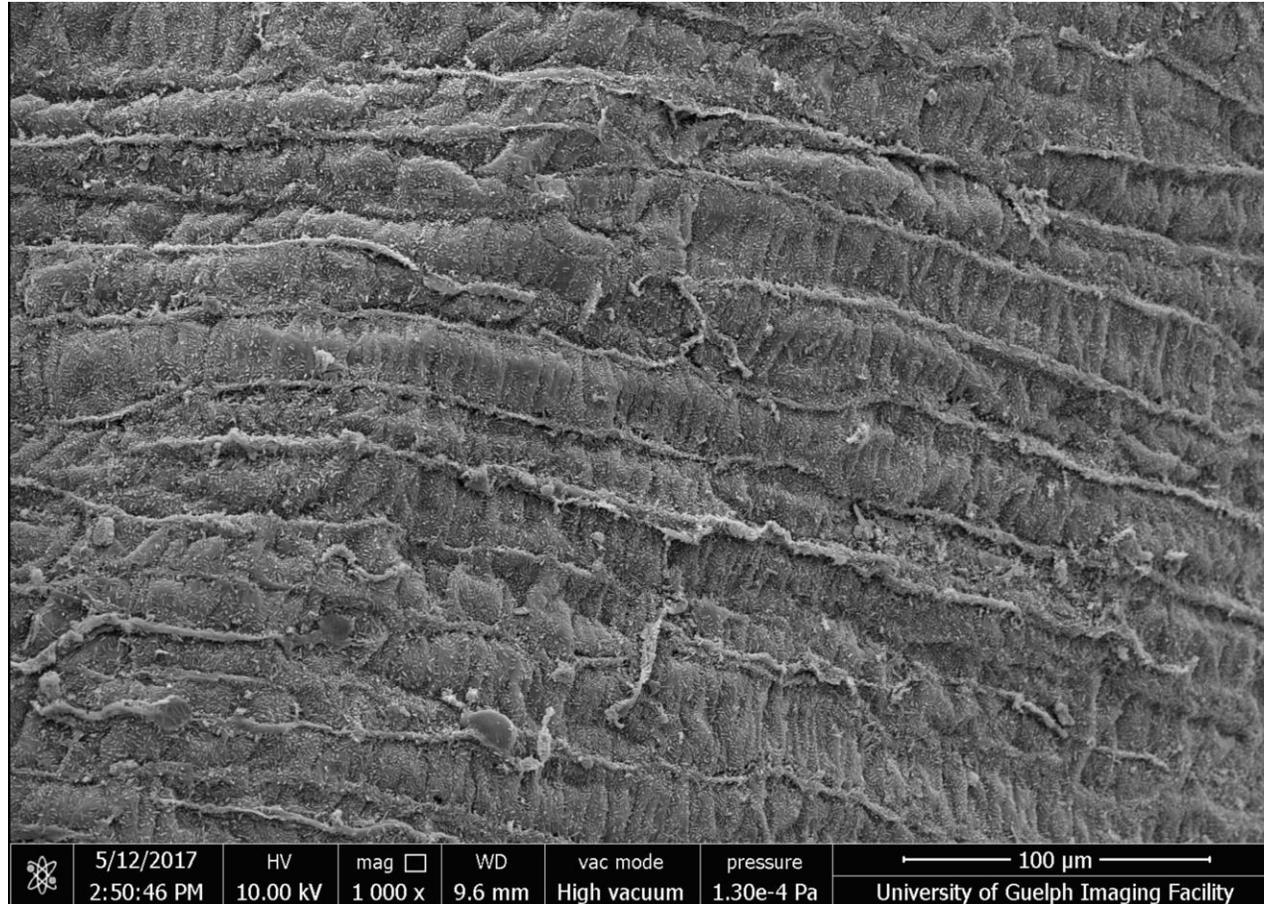
Series of scanning electron micrographs of a corn kernel retrieved from a poop sample



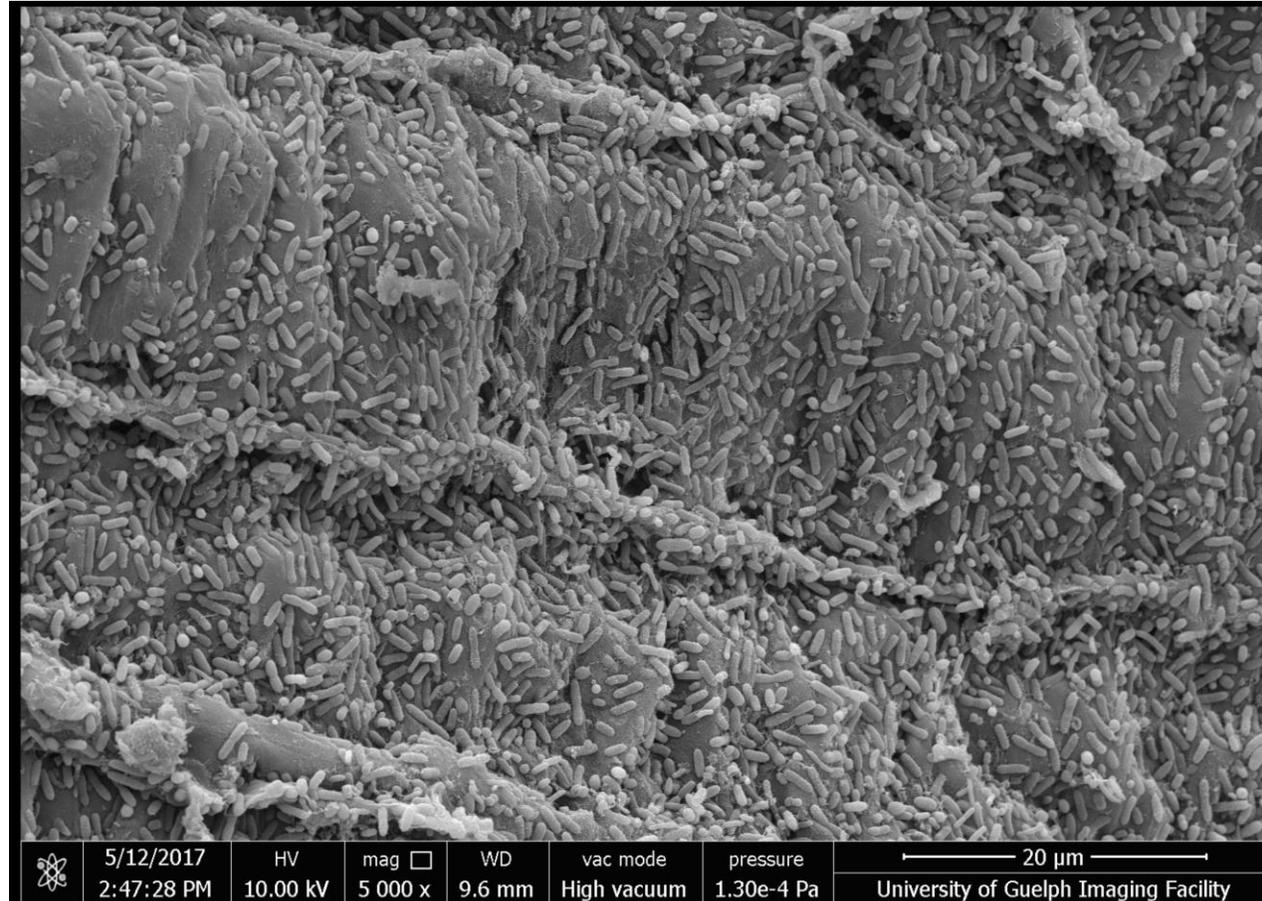
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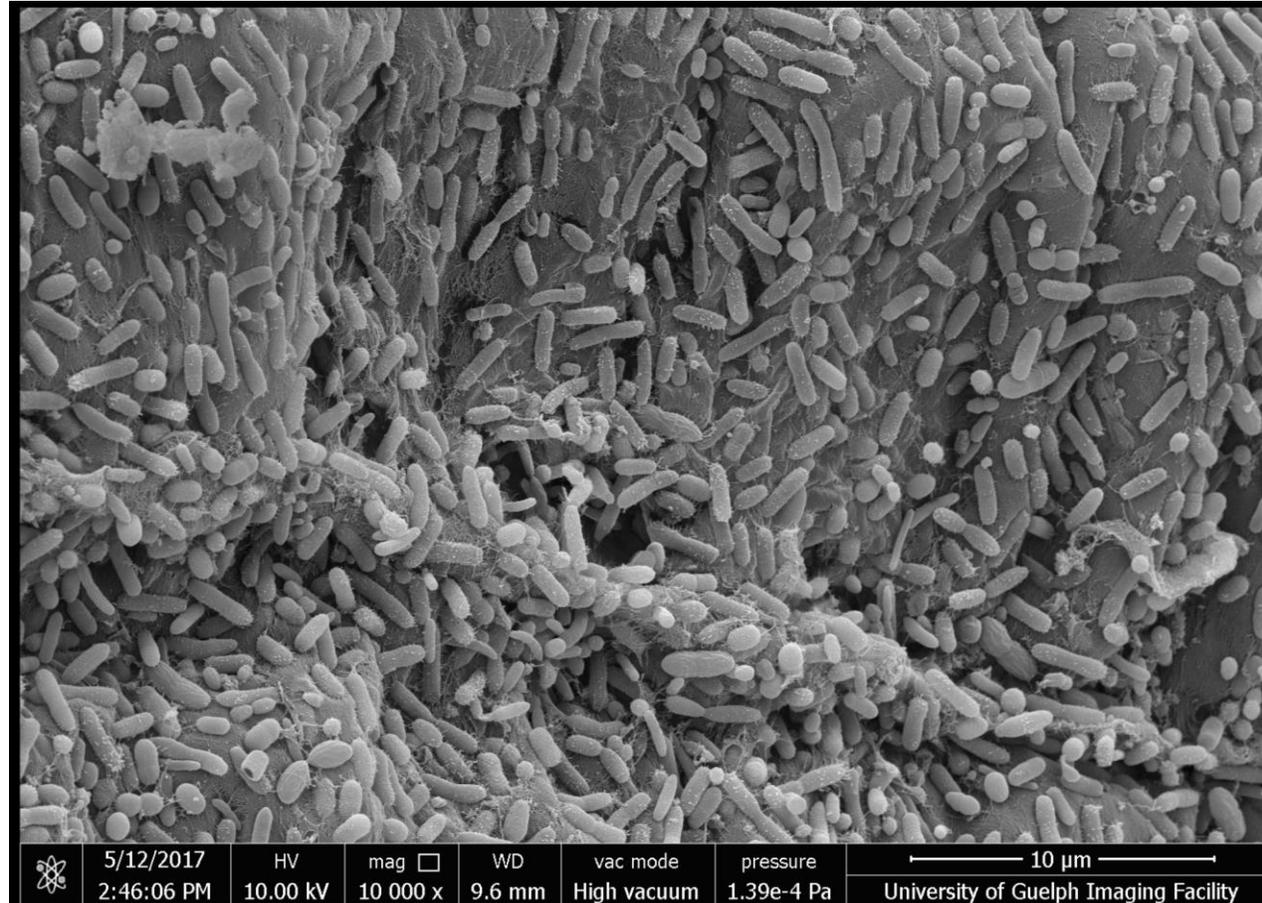
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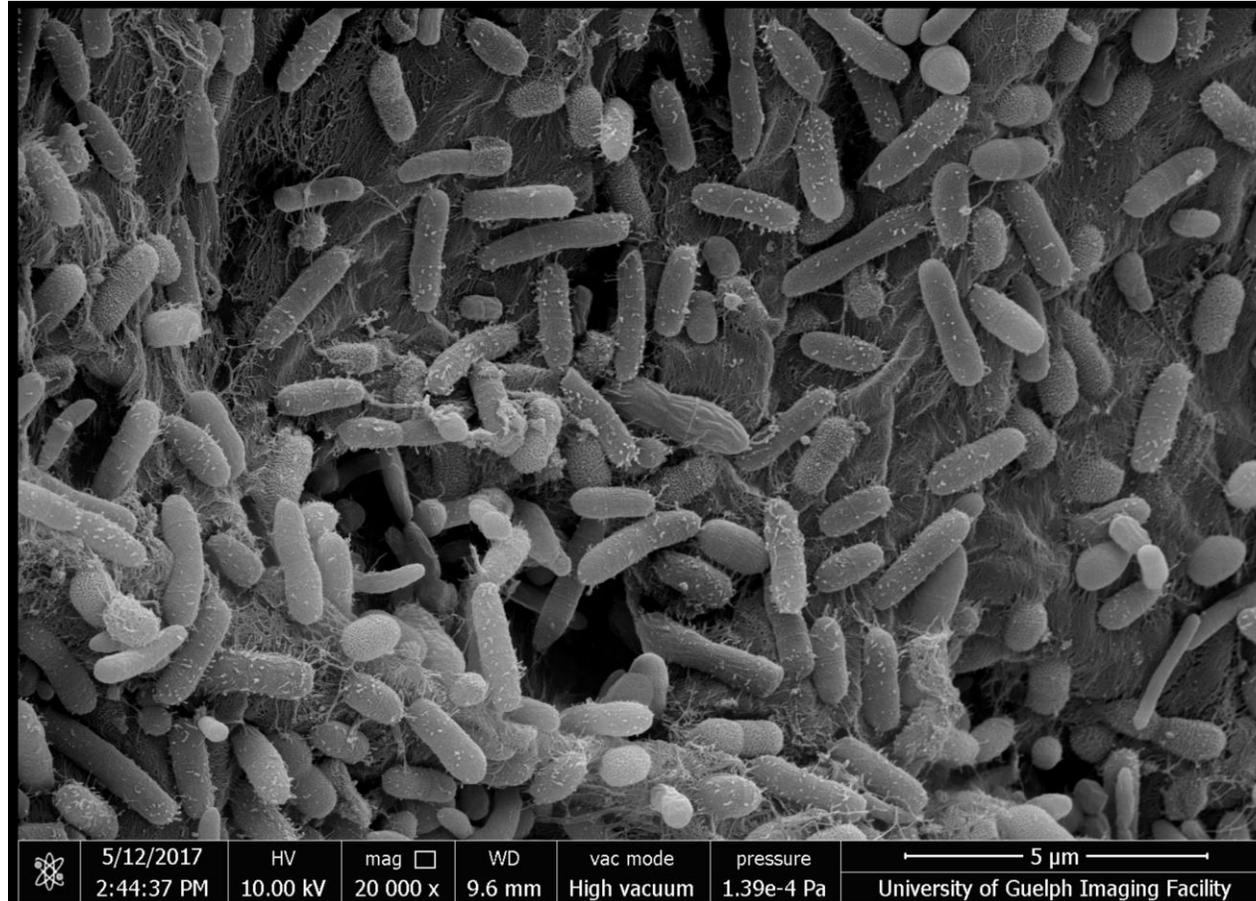
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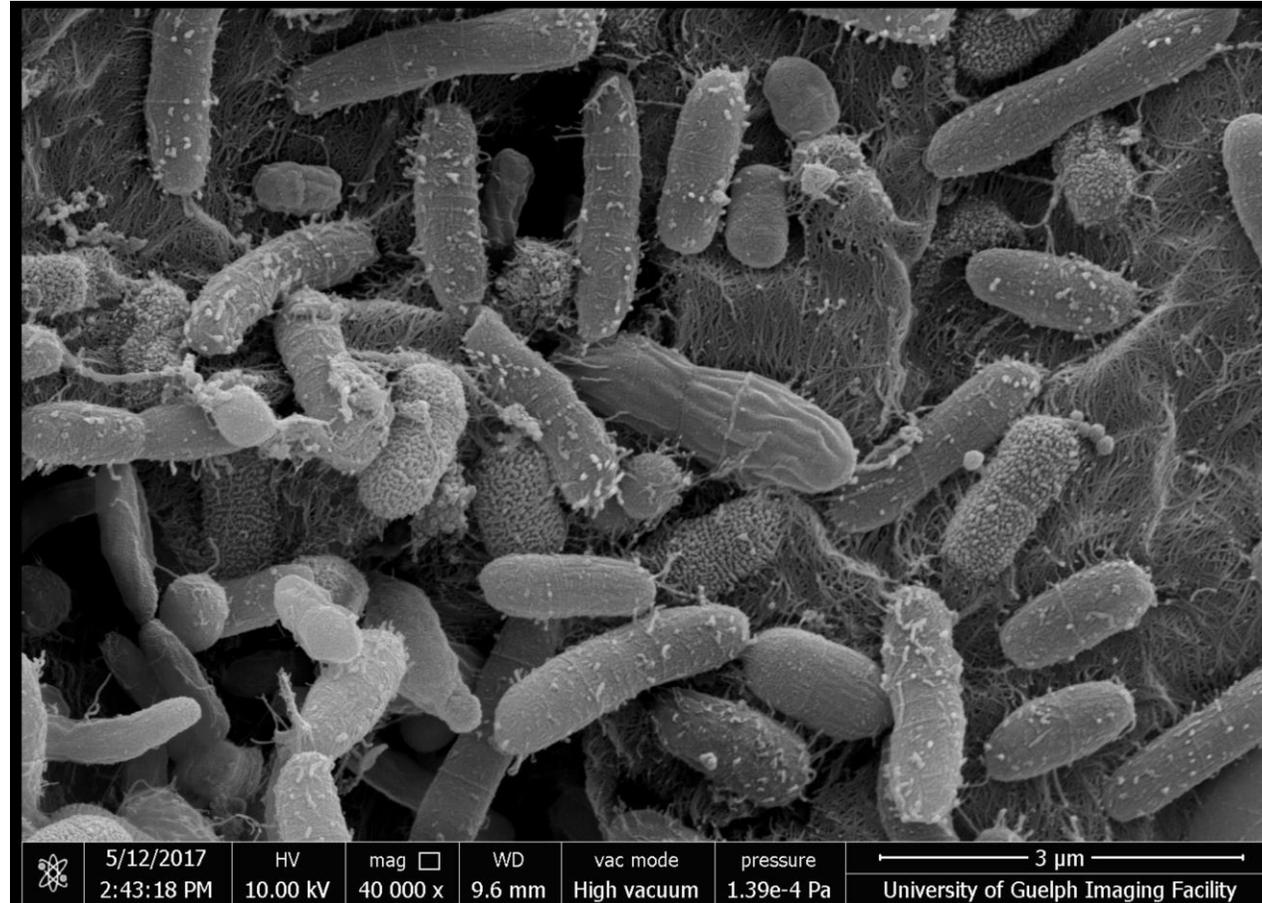
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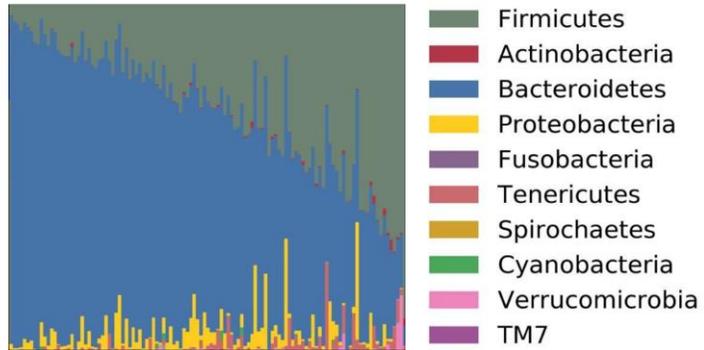
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Series of scanning electron micrographs of a corn kernel retrieved from a poop sample



Everyone is different

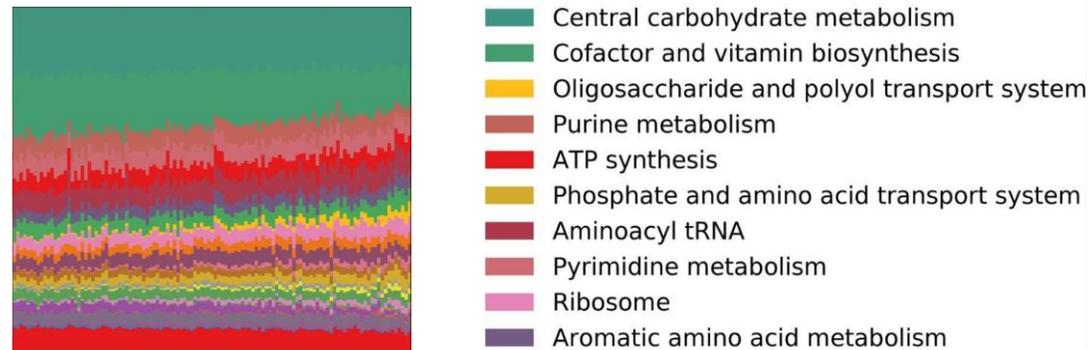


Gut microbial ecosystems are highly variable in composition and abundance profiles between people

Like a fingerprint, you have a 'pooprint'!



But ...microbial function is similar



Biodiversity in the gut is important

High diversity of species:

- Robust ecosystem
- Balance
- Functional redundancy
 - High gene count
- Resistance to damage



Low diversity of species:

- Fragile ecosystem
- Imbalance
- Functional disability
 - Low gene count
- Susceptibility to damage



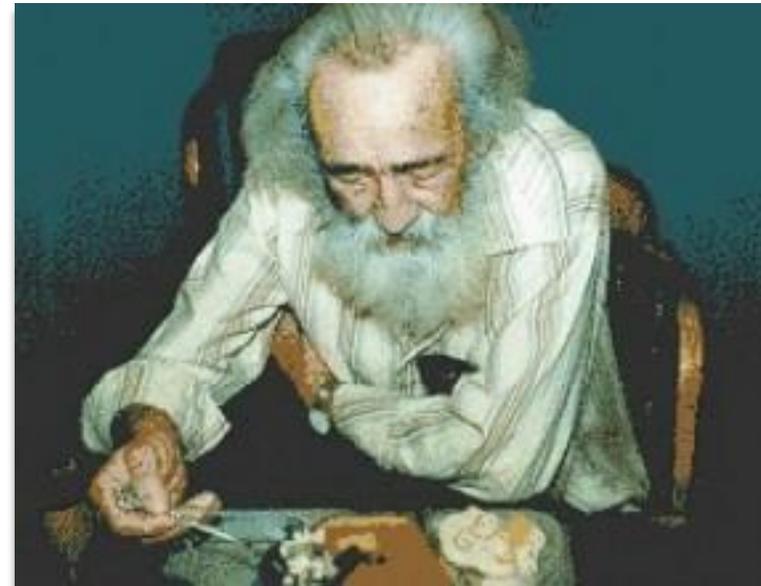
Remarkably...

The bacterial community in your gut remains stable from

- weaning...



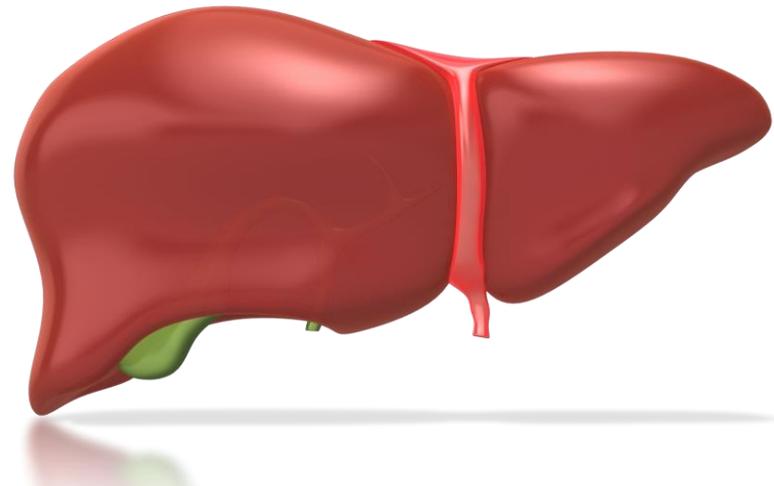
- ...to old age



- This is a combination of host and microbe-driven effects
- The window for gut microbiota development is narrow

What do our gut microbes do for us?

- Regulate the immune system
 - Help to extract energy from foods
 - Control potential pathogens
 - Make some essential metabolites, including vitamins and cofactors
 - Improve intestinal function
 - Remove toxins and carcinogens
-
- As important to us as a liver
 - A 'virtual organ'



Are we damaging our health by eroding microbiome diversity?

- Hygiene hypothesis (Strachan, 1989)
 - Lack of exposure to certain infectious agents during childhood drives allergic disease
- Old friends hypothesis (Rook, 2003)
 - Humans are dependent on a co-evolved microbiome to educate the immune system and prevent inflammatory disease
- Missing microbiota hypothesis (Blaser & Falkow, 2009)
 - Loss of microbiota generally compounds over generations, and *recent changes in lifestyle* have greatly exacerbated this loss



Artificial sweeteners...

- Artificial sweeteners influence the composition and function of your gut microbes
- They can actually promote metabolic disease
 - the very problem they were introduced to combat!



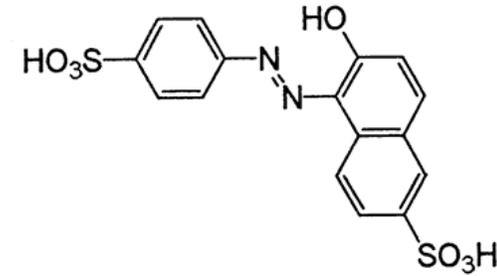
Food emulsifiers...



- Common emulsifiers carboxymethylcellulose and polysorbate-80 act like detergents in the gut
 - Disturb the mucus layer
- Change the composition of the gut microbiome
 - Shifts towards a pro-inflammatory, obese type phenotype

Artificial food colours

- Azo dyes in particular have the potential for much harm
- Considered safe because they are 'stable', but gut microbes can easily metabolize them!
 - A current focus of the A-V lab



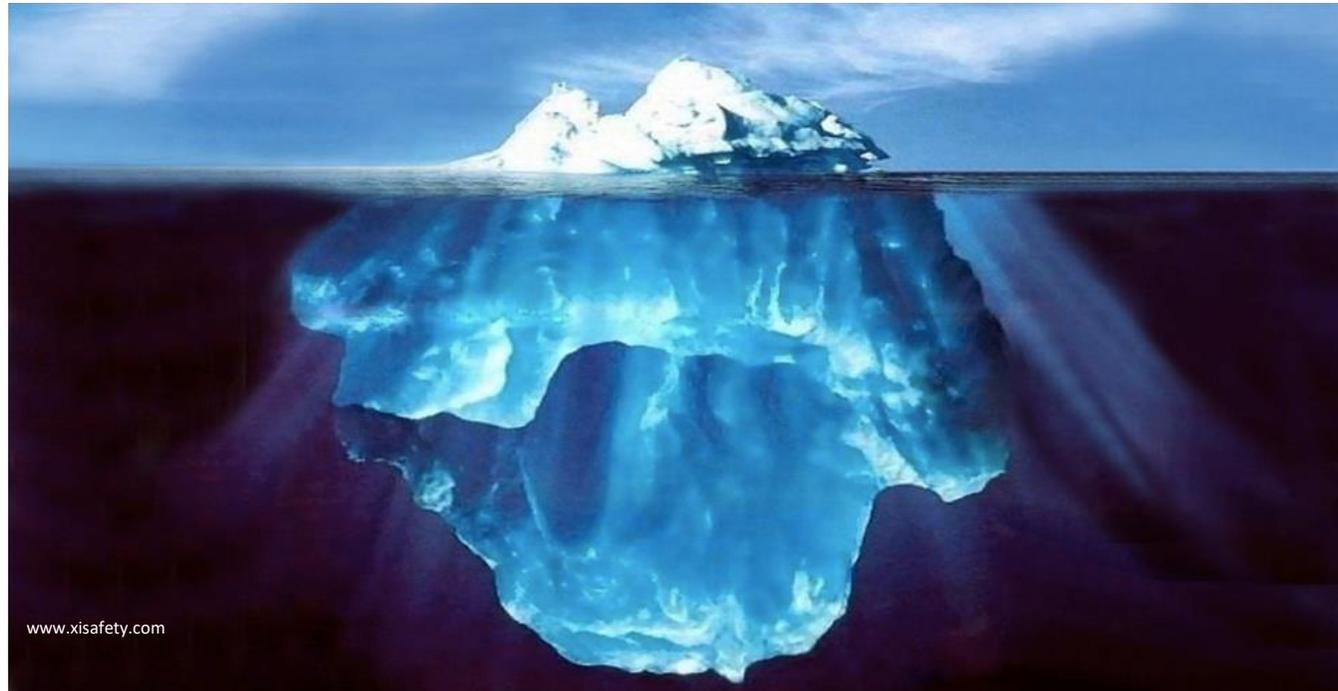
What about common drug products?



- Why do some drugs work miracles in some patients and do nothing for others?
- We've been focusing on the wrong genome!
 - Remember, your gut microbiome carries out a great deal of metabolic 'work' for you!
- Everyone's gut microbiome is different... so predicting drug effects suddenly becomes a lot more complicated!
- There is a new era of pharmacology emerging: 'metagenomic toxicology'

What we *need to understand*:

- The safety of many food additives, supplements and drugs has NEVER been assessed taking into account our microbial passengers
 - we are just scratching the tip of the iceberg



How do we know that Westerners have low gut diversity?

- We **can't** go back in time to look at microbiomes pre-antibiotics/refined foods
- We **can** look at indigenous peoples who have not had exposure to these things



Their gut microbiomes are *much* more diverse than ours!

Examples of diseases *associated* with altered gut microbiota diversity (published research)

Infant colic **Inflammatory bowel diseases**
Autism **Eczema** **Colorectal cancer**
Allergic asthma **Obesity**
Parkinson's disease
Neonatal necrotizing enterocolitis
Irritable Bowel Syndrome **Diabetes**
***Clostridioides difficile* infection**
Depression and anxiety

The pervasive advertising message is
“all microbes are bad!”



But only a
tiny fraction
of microbes are
pathogens

Antimicrobial practices don't discriminate between pathogens and microbiota

This situation is starting to change!

Germ-Killing Brands Now Want to Sell You Germs

The world's best-known antibacterial labels are pouring millions into probacterial health and beauty startups



Bloomberg Businessweek

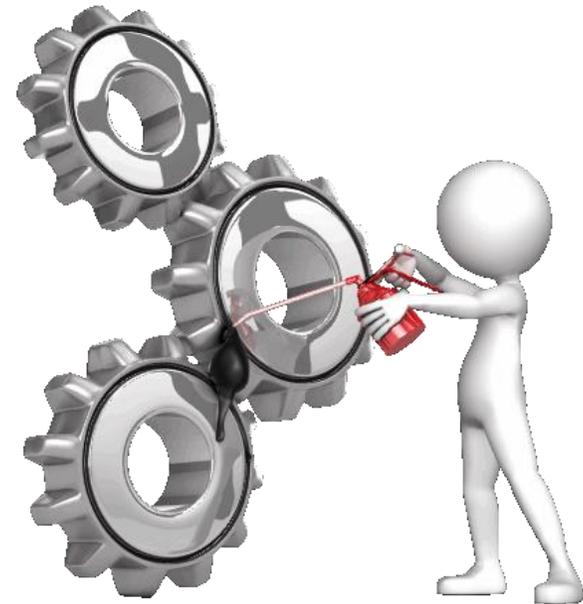
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How can we 'fix' dysfunctional gut microbial ecosystems?

Probiotics, prebiotics and beyond...



Can we fix dysbiosis with probiotics?

- If you take an antibiotic, you can just cancel the negative effects out by using a probiotic, right?
 - Nope!
- Many types and strains of probiotics
- Many manufacturers, some legitimate, most not
- Many over-inflated claims
- Very little actual science

Study of 14 commercial probiotic products¹ showed:

“...many probiotic products contain unadvertised additional lactobacilli and bifidobacteria, whereas others are missing species listed on the product label.”
Many probiotic capsules contain far fewer than the number of microbial cells advertised.

1 Marcobal et al. J Pediatr Gastroenterol Nutr. 2008 May;46(5):608-11.

The layperson's view of probiotics...



Myth 1:
Probiotics found in food
are the same kinds of
species that are found
in the gut

Myth 2:
Probiotics colonize the
gut

The microbial ecologist's view of probiotics



Normal gut microbiota

Colon: 100 billion to 1 trillion CFU per mL

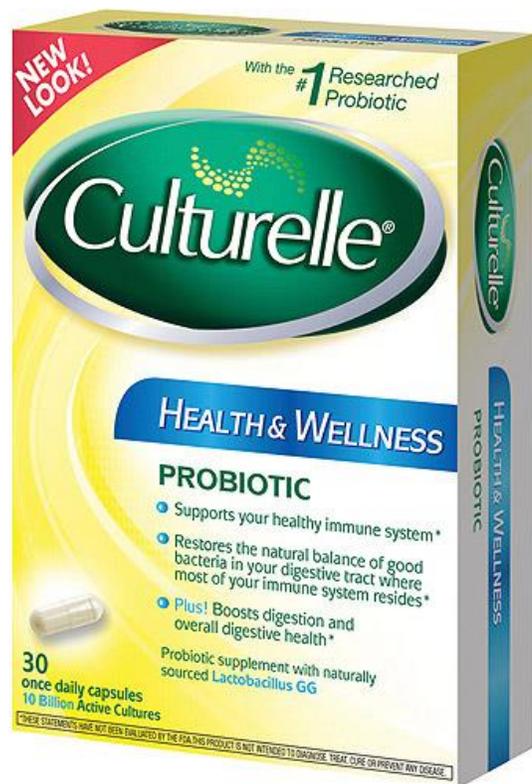
vs.



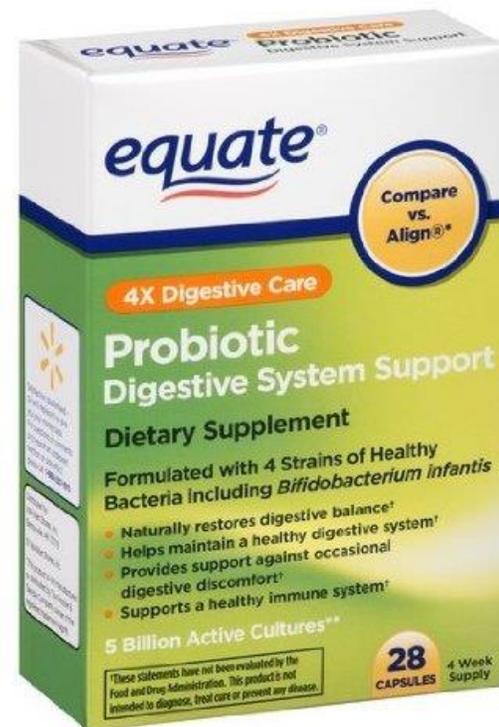
Probiotic

2-15 billion CFU per capsule

Strain is important, not just species!



Clinical evidence for efficacy
Probiotic species and *strain* clearly labeled



No clinical evidence for efficacy
Probiotic species, but no strain on the label

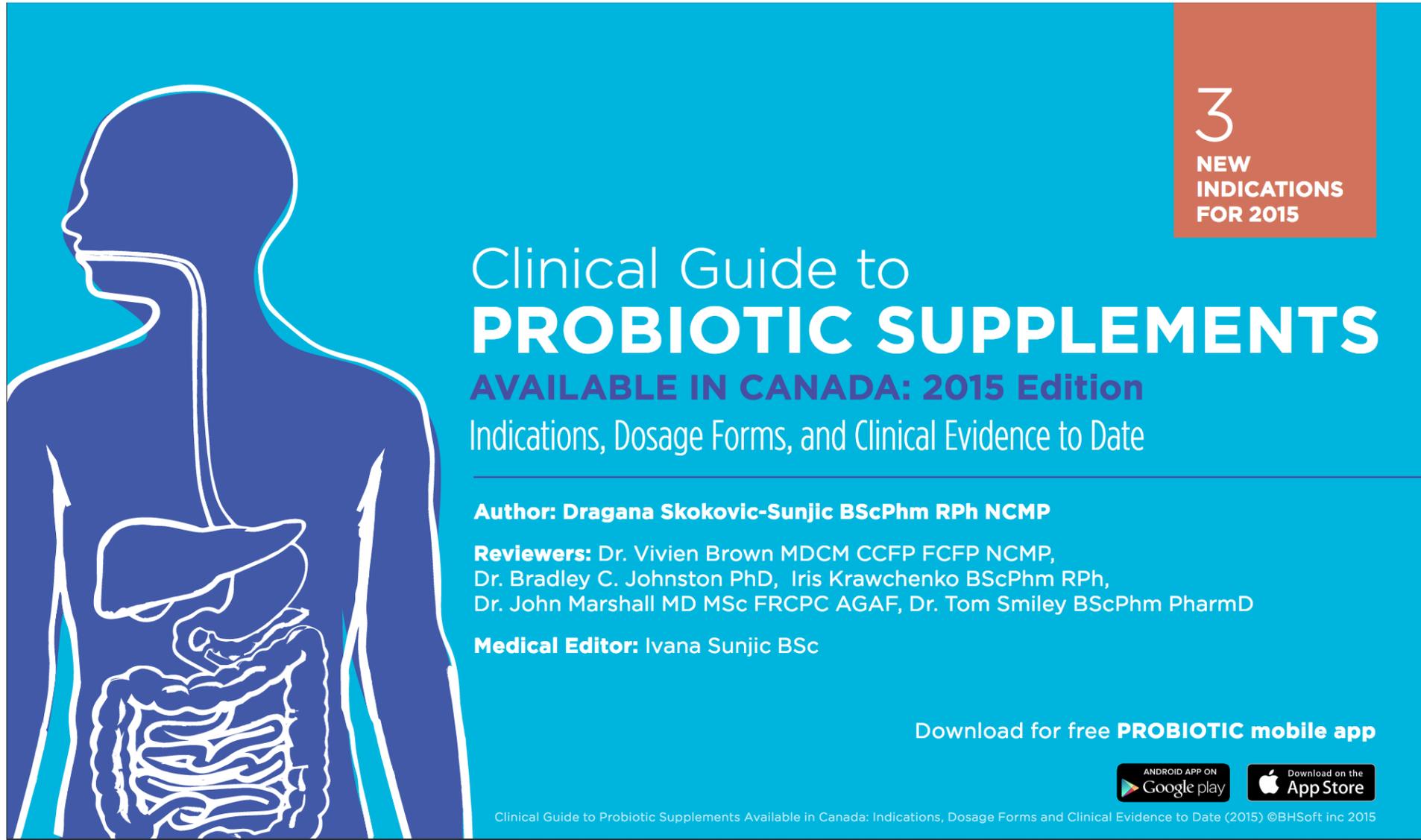
Be realistic...

- You would not expect to use a drug designed to treat diarrhea for the treatment of psoriasis
 - So don't assume probiotics are panaceas, either!
- Benefits seen in clinical trials are generally modest, at best
- But the risk of side effects is very low, so worth a try **IF** you pick the right probiotic!



My advice: do careful research or consult
reputable sources for info

<http://www.probioticchart.ca/>



3
NEW
INDICATIONS
FOR 2015

Clinical Guide to **PROBIOTIC SUPPLEMENTS**

AVAILABLE IN CANADA: 2015 Edition
Indications, Dosage Forms, and Clinical Evidence to Date

Author: Dragana Skokovic-Sunjic BScPhm RPh NCMP

Reviewers: Dr. Vivien Brown MDCM CCFP FCFP NCMP,
Dr. Bradley C. Johnston PhD, Iris Krawchenko BScPhm RPh,
Dr. John Marshall MD MSc FRCPC AGAF, Dr. Tom Smiley BScPhm PharmD

Medical Editor: Ivana Sunjic BSc

Download for free **PROBIOTIC mobile app**

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Clinical Guide to Probiotic Supplements Available in Canada: Indications, Dosage Forms and Clinical Evidence to Date (2015) ©BHSft inc 2015

What about fecal transplants?

Use a healthy donor's microbes to replace your own...



- Fecal homogenate instilled into patient
- Rectal enema
- Colonoscopy
- Nasoduodenal tube
- “Crapsules” – encapsulated frozen or freeze-dried stool

- For *C.diff* infection, results in cure of the patient in **>90%** of cases
- Rapid resolution of disease
- Only rare recurrence of infection
- But there are risks associated with ‘unknown microbes’



What if we could make FMT safer?

- Couldn't we just select pure microbes from healthy stool to create a microbial ecosystem therapeutic?



Well, we did!

- ‘MET-2’ is a new, first-in-class biologic drug
- A lyophilized, standardized ecosystem for oral delivery

Clinical trials underway for rCDI,
and several other indications

Not a probiotic – will be prescription only

NUBIYOTA
BETTER ECOSYSTEM, BETTER HEALTH



To help maintain health,
remember the gut microbiota 3 R's:

- **Recognize** that we are custodians of a hidden army of helpful microbes
- **Respect** what these microbes do for us
- **Reinforce** their beneficial activities

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Keith Sherriff
Alexander Stirling
Co-founders
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National Institutes
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MINISTRY OF RESEARCH AND INNOVATION

The pervasive advertising message is
“all microbes are bad!”



But only a *tiny fraction* of microbes are pathogens

Antimicrobial practices don't discriminate between pathogens and microbiota

HAVE YOU FED YOUR GUT MICROBES TODAY?

