Appetite for Life
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Human Gut Microbiome and Diet: Whose diet is it anyway?

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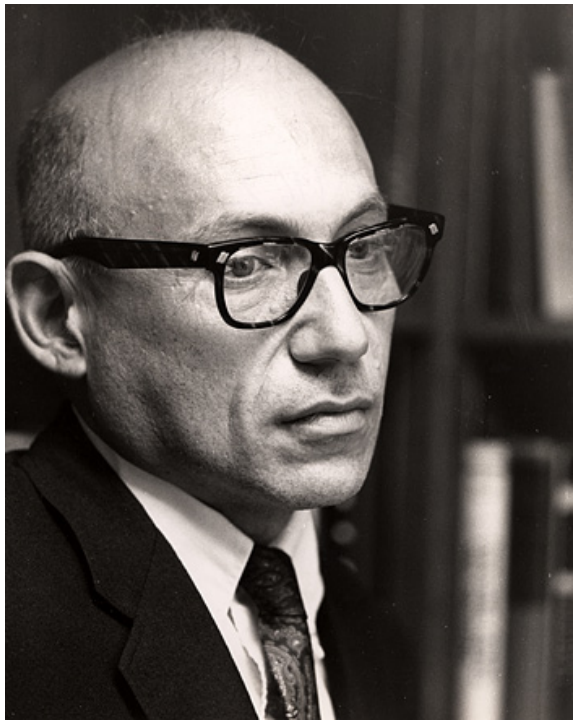
Outline

- What is the microbiome?
- How is it characterized?
- How does it develop?
- What affects it?
- How does it affect responses to diet?
- How is it associated with health and disease?

What is the microbiome?



"The ecological community of commensal, symbiotic, and pathogenic microoganisms that literally share our body space."

Joshua Lederberg

1925-2008

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Lederberg and McCray, *The Scientist*, 2001

The Gut Microbiome: What have we learned?

- It's complex.
- Trillions of microorganisms in human body
- Microbiome has 100 times as many genes as the human genome
- Important symbiosis between human host and microorganisms

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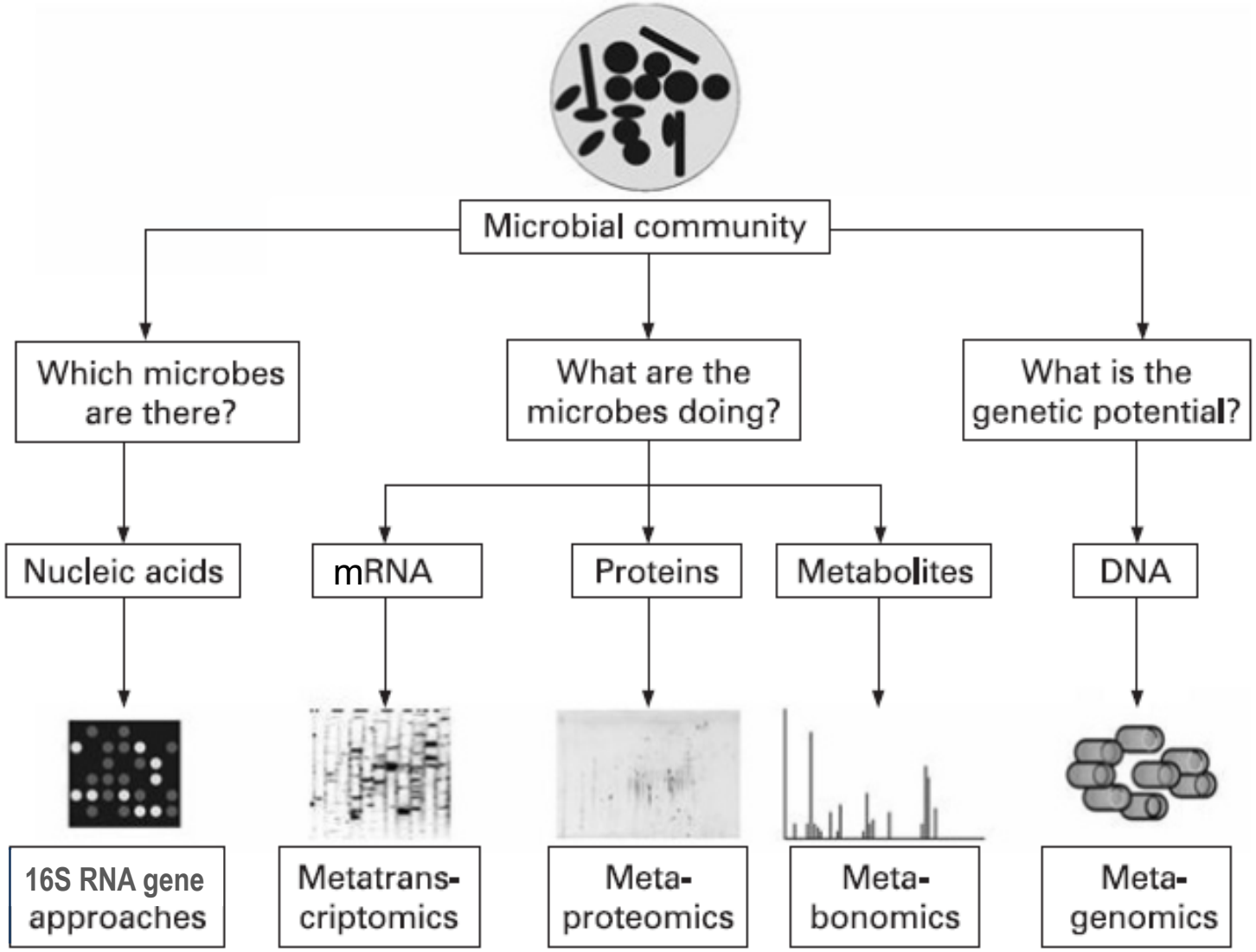
Sender et al. *PLOS Biol* 14(8):e1002533, 2016

The Gut Microbiome: Who is there?

- Bacteria
- Viruses
- Protozoa
- Fungi

Characterizing the Gut Microbial Community: Who is there and what are they doing?



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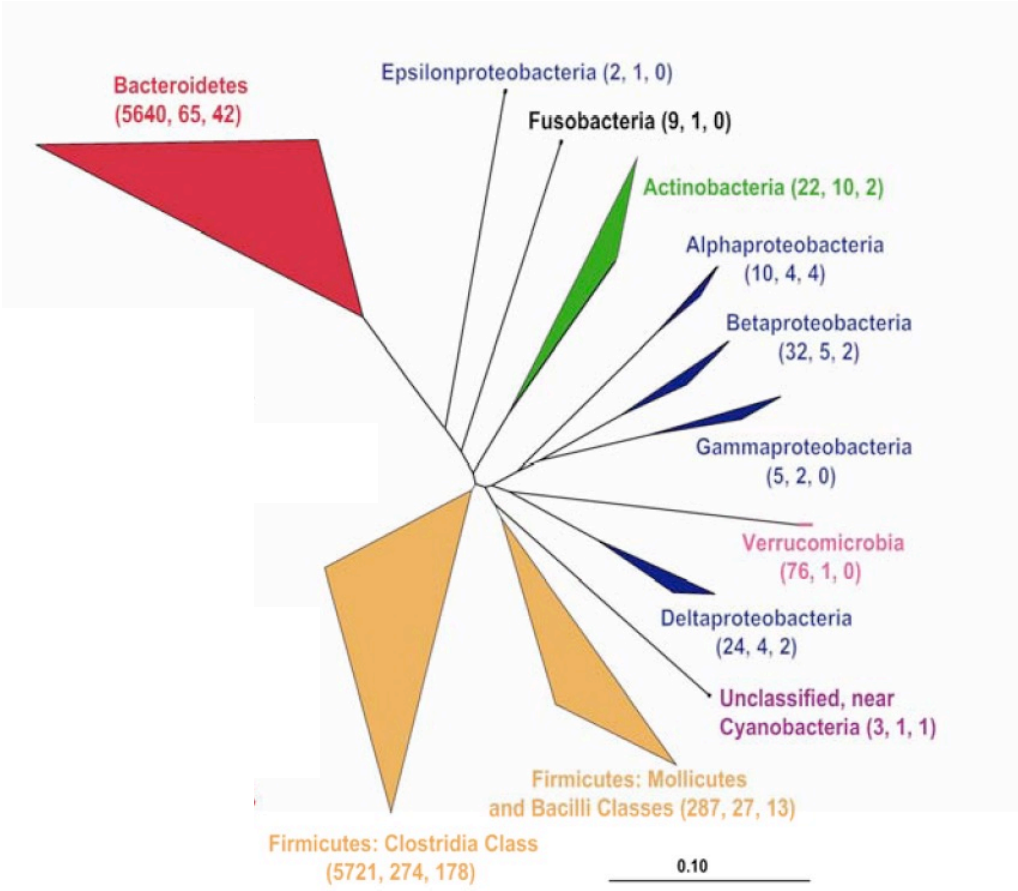
Zoetendal et al., *Gut*, 2008

Bacterial Diversity in the Adult Human Gut

Kingdom • Phylum • Class • Order • Family • Genus • Specie

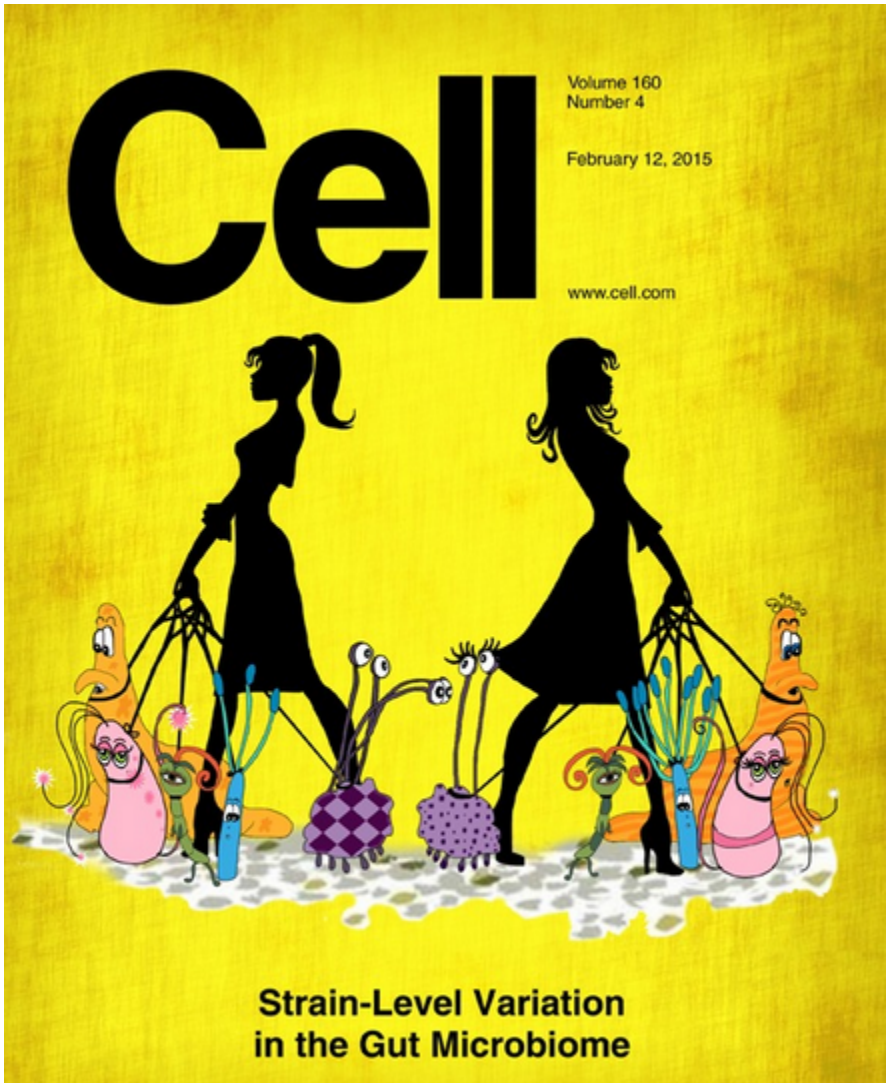


- At least 10 different phyla of bacteria found in the human gut
- 5 phyla represent majority of bacteria
- Bacteroidetes and Firmicutes dominate.

Bäckhed et al. *Science* 2004
Marchesi et al, Gut, 2016

Much of the variation in the gut microbiome occurs at species and strain level

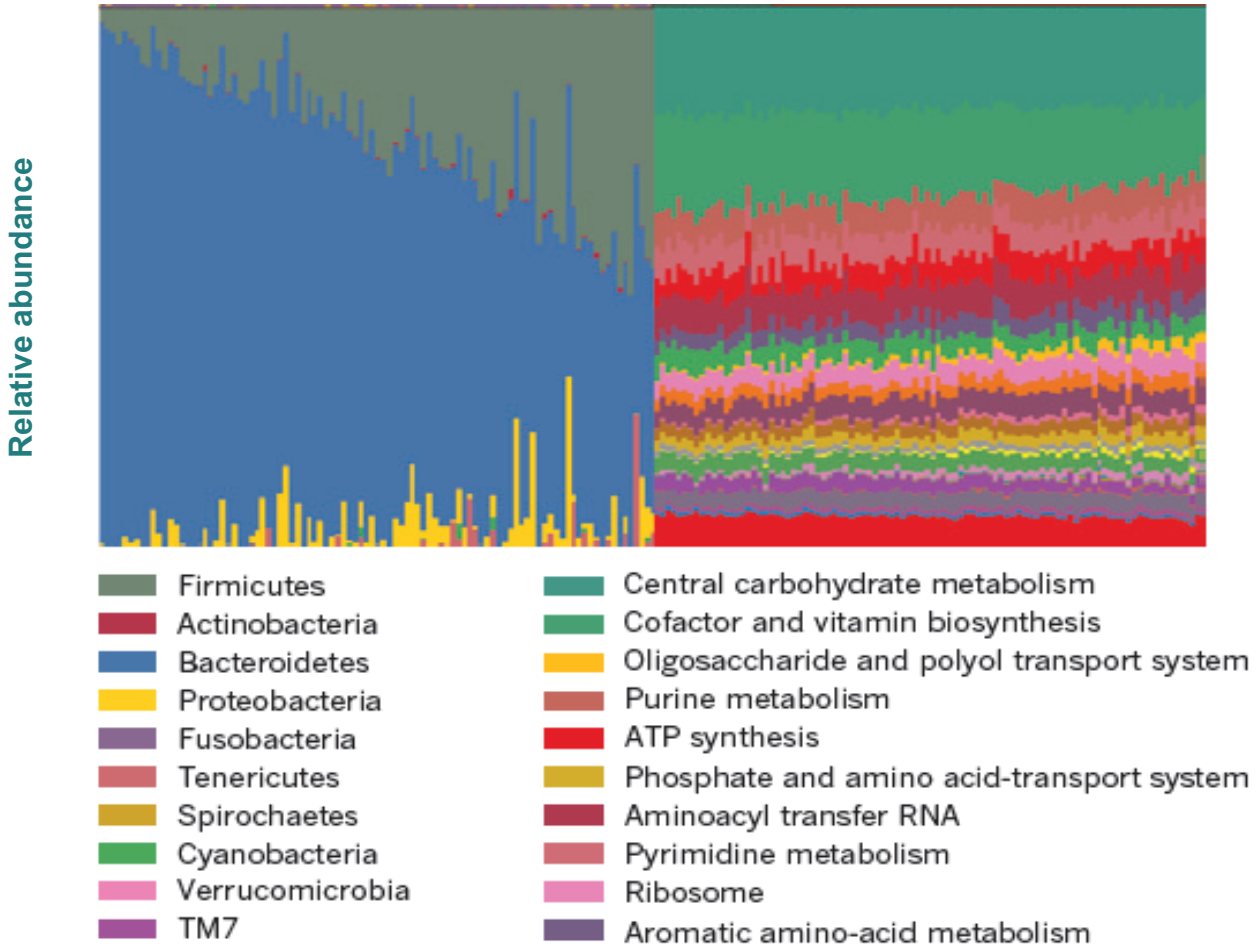
Kingdom • *Phylum* • *Class* • *Order* • *Family* • *Genus* • ***Species***



- 500-1000 species in the human gut
- Gut microbial community structure is specific to an individual
- A healthy adult human gut microbial community is relatively stable.

Comparison of Structural (Taxonomic) and Functional Variation in the Human Gut Microbiome

Who is there? What is their functional potential?



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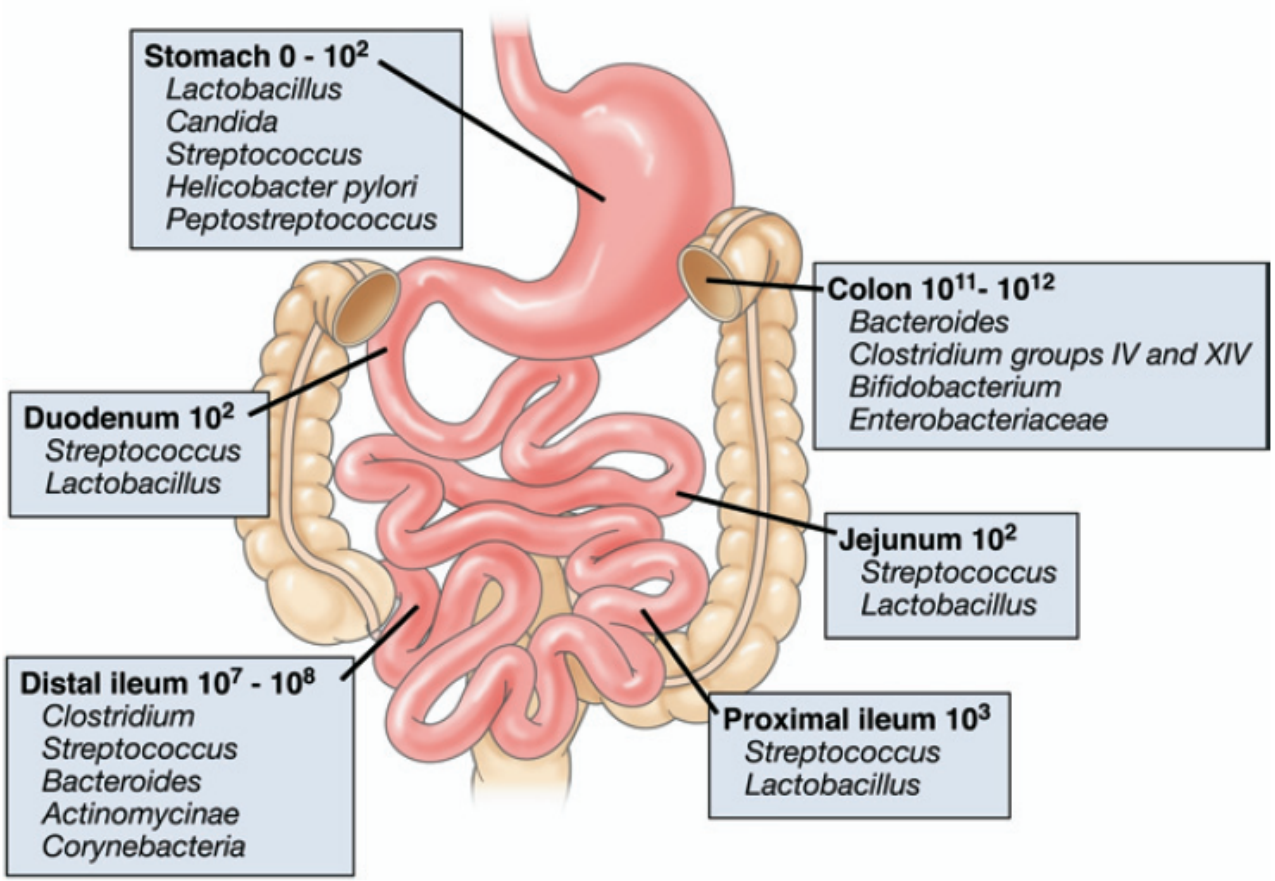
Human Microbiome Project Consortium. *Nature* 486:207, 2012

The Human Gut Microbiome

Composition and luminal concentrations of microbial groups vary along the GI tract.



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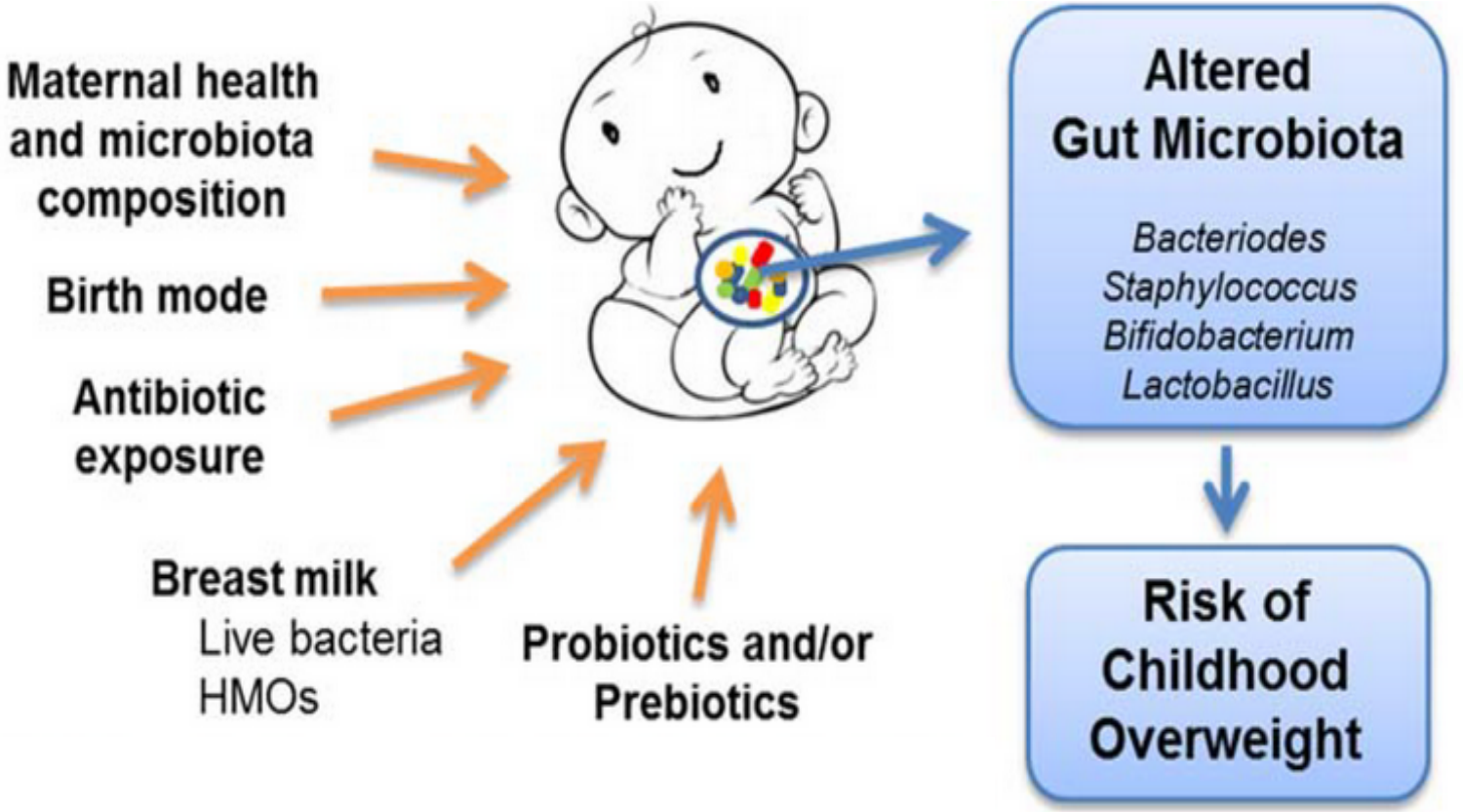
Sartor RB, *Gastroenterol*, 134:577,2008

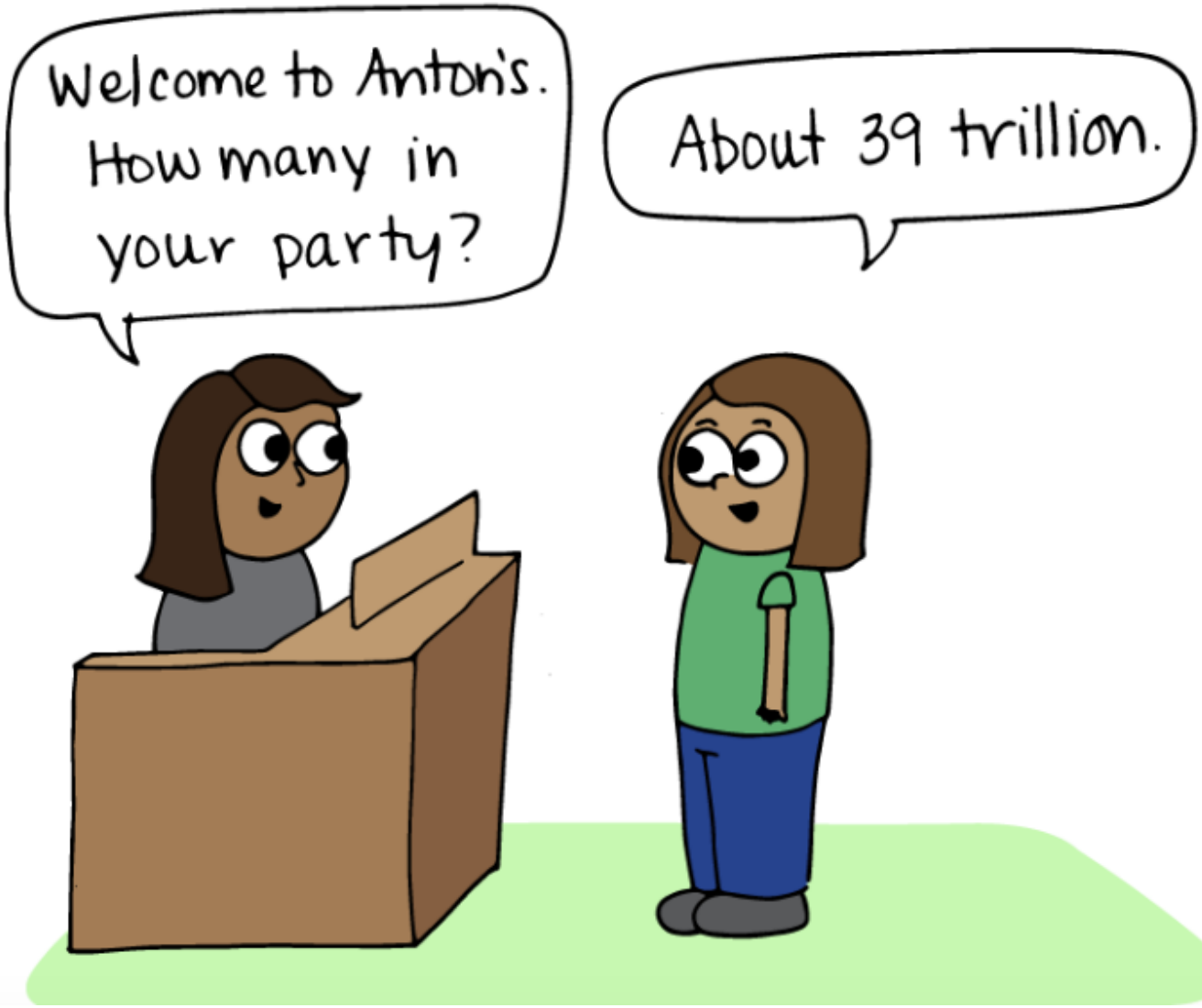
How does the microbial community develop?

Ottman N et al, *Front Cell Infection Microbiol*, 2012

Factors that may modify infant gut microbiome

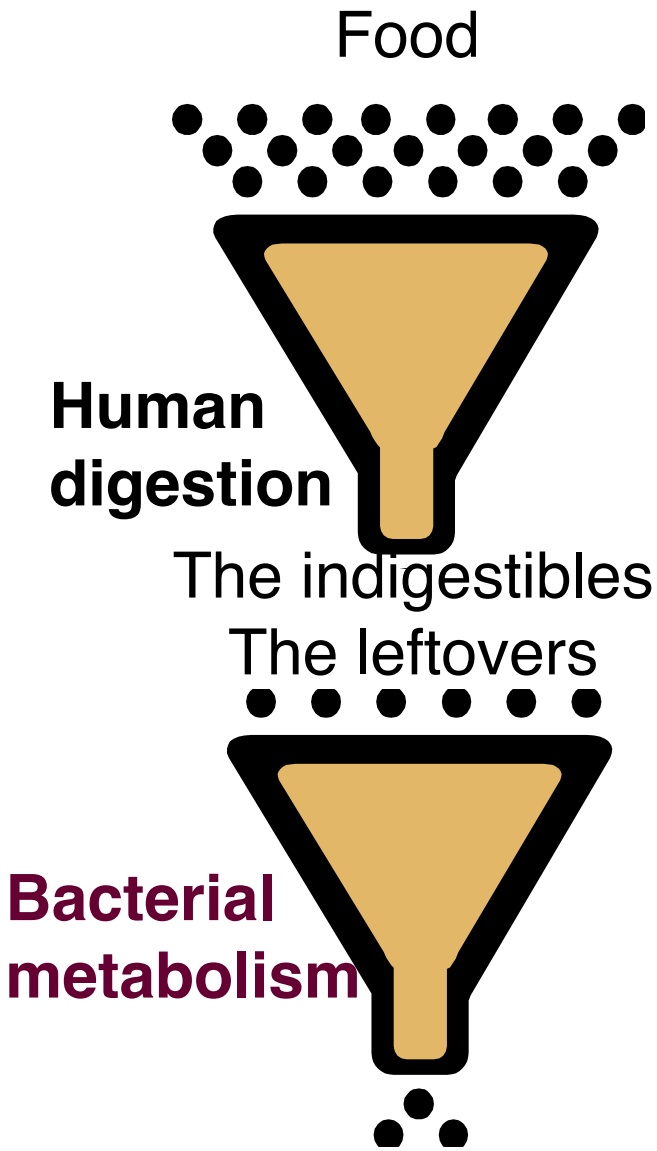


Feeding the Gut Microbiome

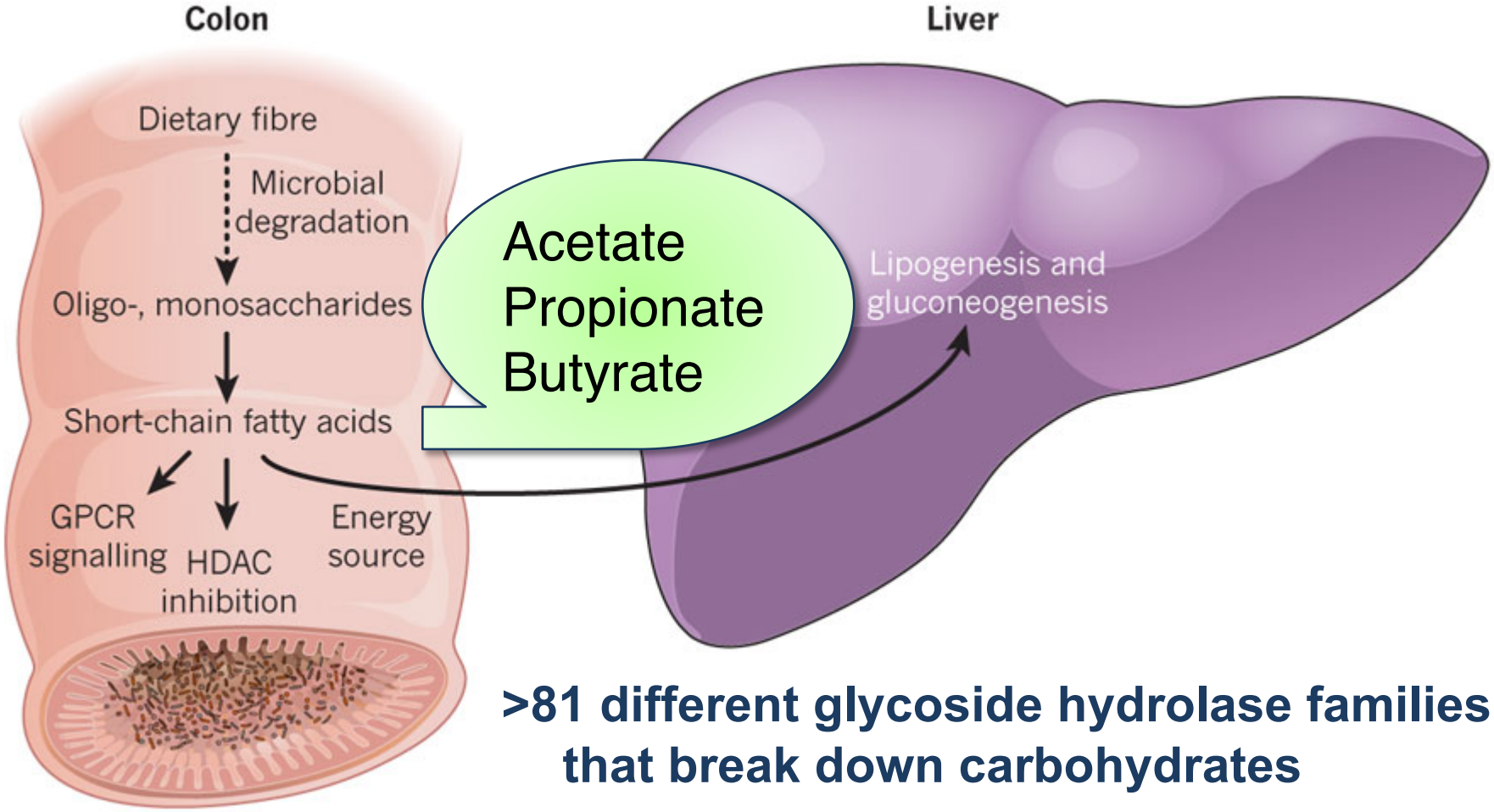


Gut Microbial Metabolism

- Obtain energy and nutrients to live and reproduce
- Microbiome: >100 times as many genes as human genome
- Carry out reactions that human gut enzymes cannot:
  - Fermentation
  - Denitrification
  - Sulfate reduction
  - Aromatic fission
  - Hydrolysis/deconjugation



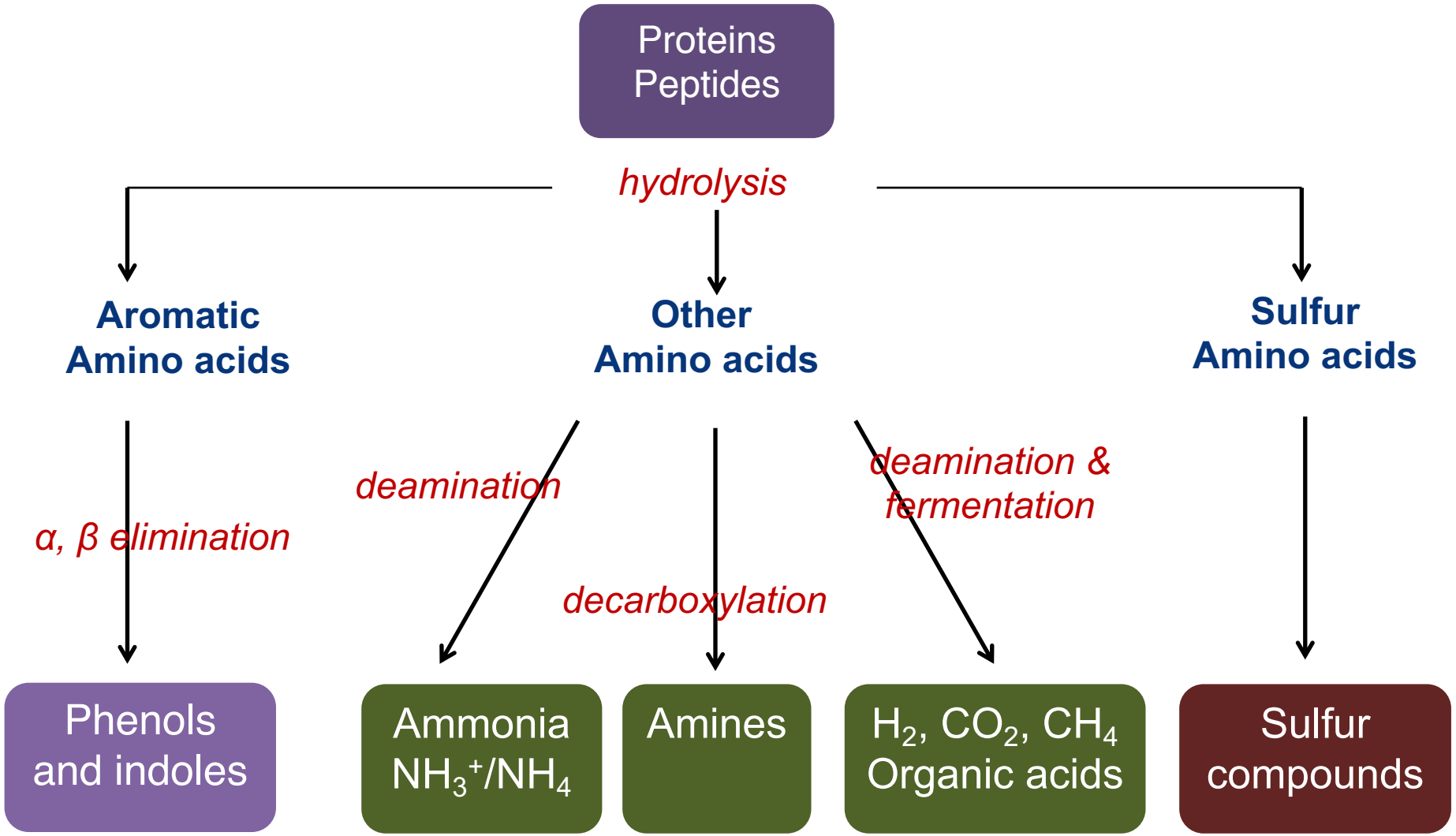
Fermentation of Carbohydrates:
Sugars, Dietary Fiber and Resistant Starch



>81 different glycoside hydrolase families that break down carbohydrates

Gill et al, *Science*, 2006
Tremaroli & Bäckhed, *Nature*, 2012

Microbial Metabolism of Proteins & Amino Acids



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Adapted from Nyangale et al. *J Proteome Res,* 2012

How does diet affect the gut microbiome?

Evidence from:

Observational studies

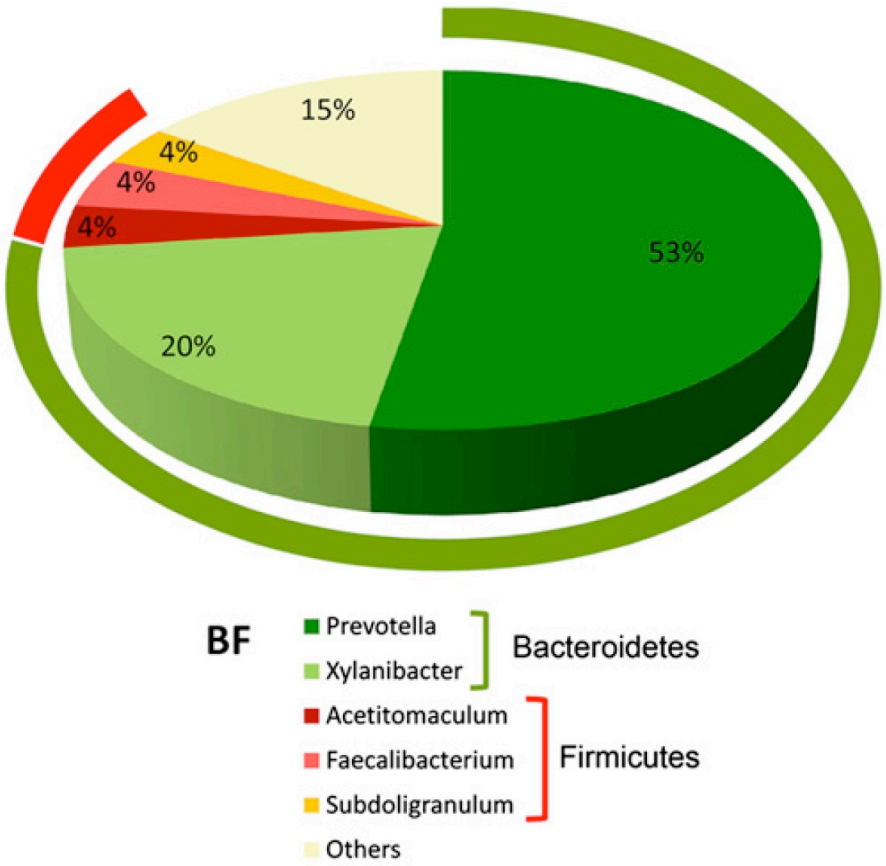
- Globally distinct populations
- Long-term food pattern consumption

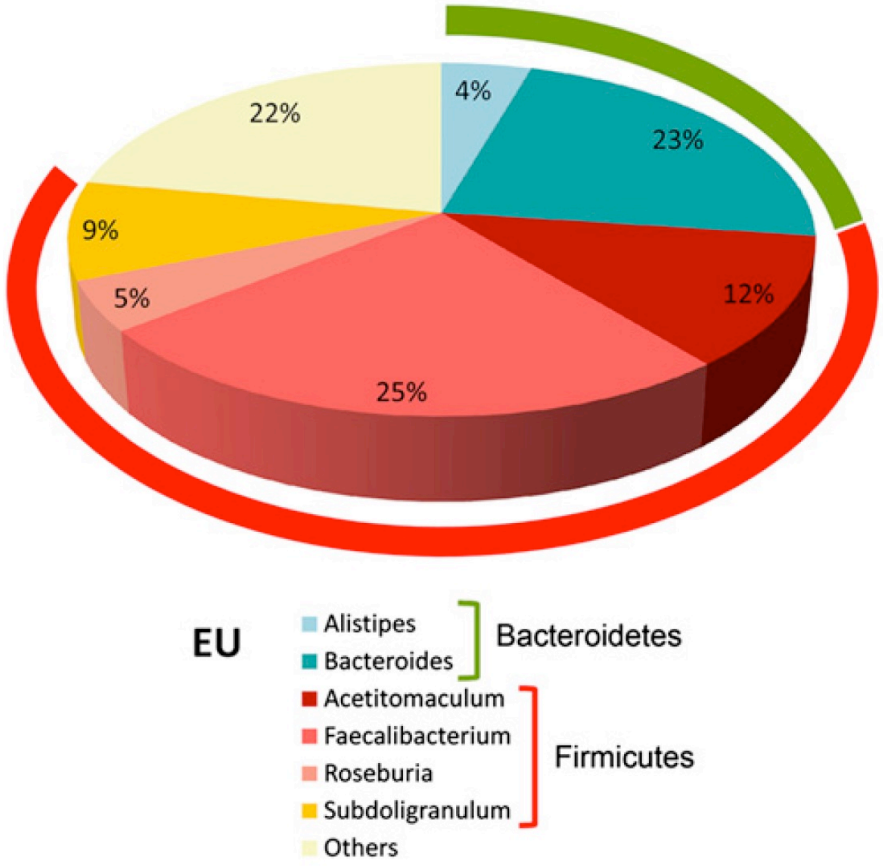
Dietary interventions

- Controlled feeding studies

Reviewed in Arora & Bäckhed. *J Int Med* 280:339, 2016

Global Population Differences: Children in Rural Africa (BF) vs Urban Europe (EU)





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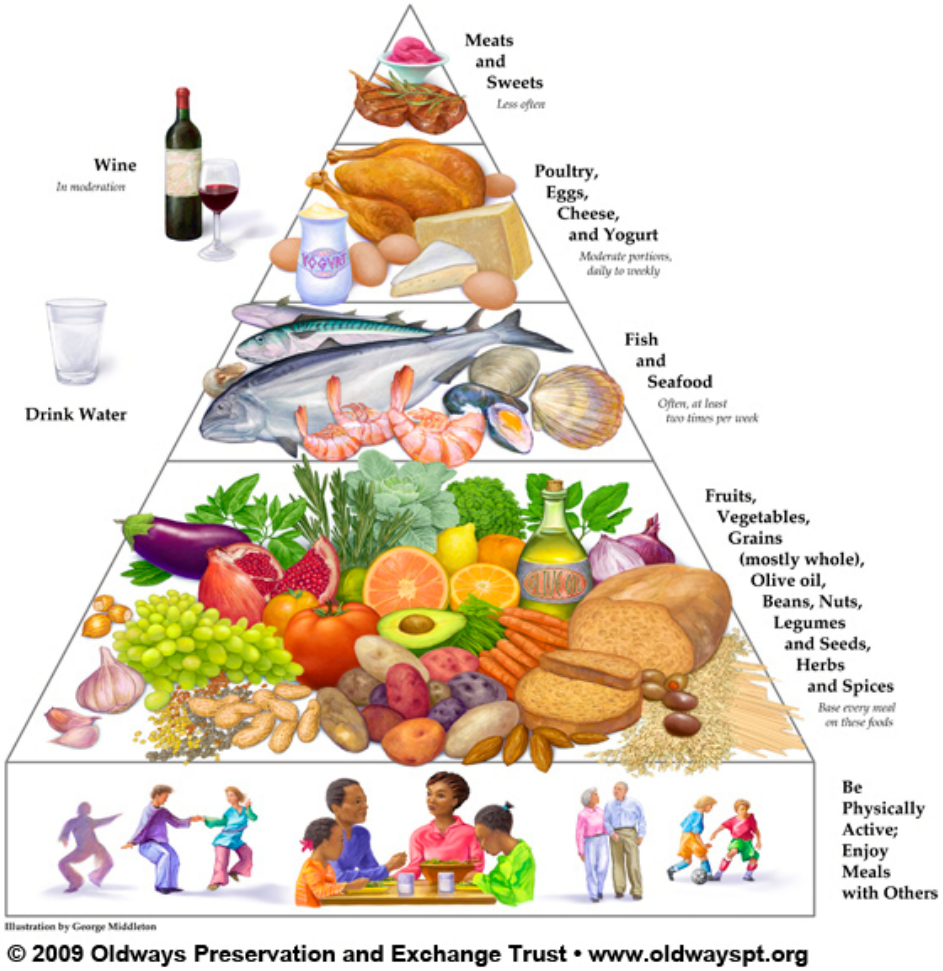
De Filippo et al *PNAS* 107:14691, 2010

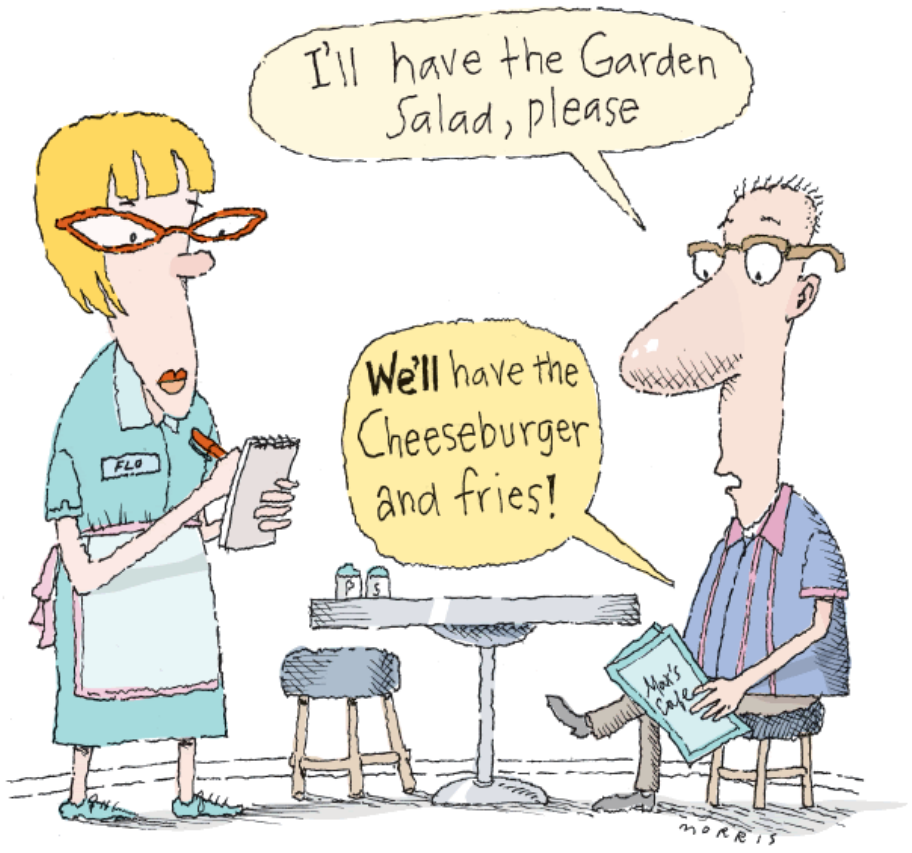
Dietary Patterns and Gut Microbiome

Mediterranean Pyramid



- Dietary Patterns:
  - Healthy Eating Index 2010
  - Alternative Healthy Eating Index
  - Mediterranean diet
  - DASH diet
- To date, few studies have examined associations between specific healthy eating patterns and the gut microbiome.

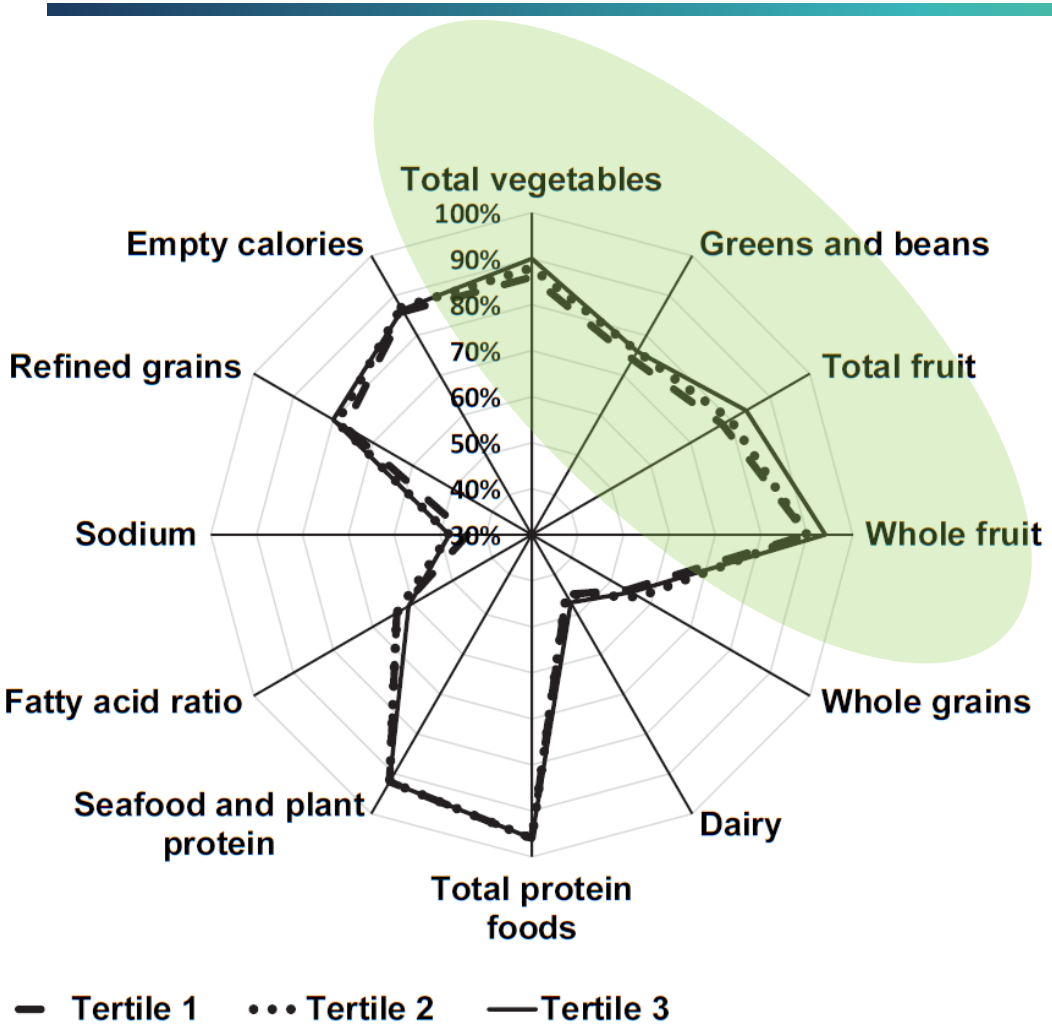
Dietary Patterns for Human Health and Gut Health



A healthy eating pattern includes:

- A variety of vegetables from all the subgroups
- Fruits, especially whole fruits
- Grains, at least half of which are whole grains
- Fat-free or low fat dairy
- A variety of protein foods, including … legumes, and nuts and seeds and soy products.
- Oils

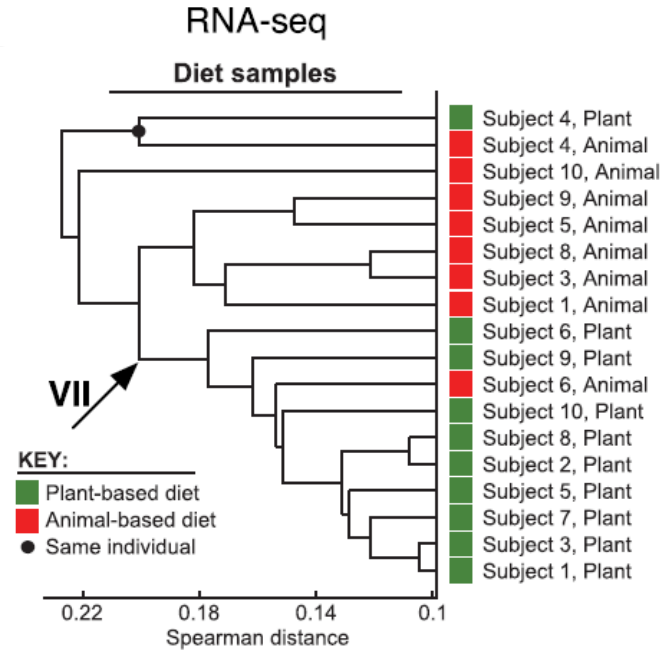
Fecal Microbial Diversity and Structure Associated with Diet Quality

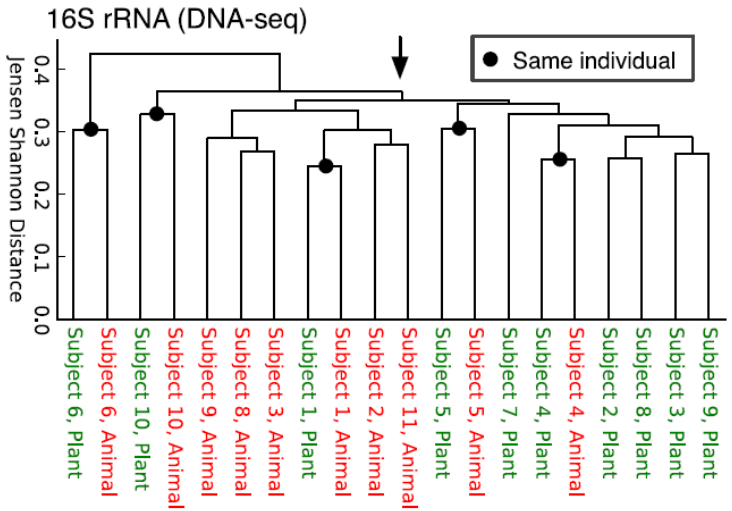


- 1735 participants in the Multiethnic Cohort
- Higher diet quality was associated with greater microbial community diversity.
- Intake of fruit and vegetables was an important contributor to the diversity.

Maskarinec …. Lampe, *J Nutr*, in press

Short-Term Feeding of Plant- and Animal-based Diets Alters Gut Microbiota

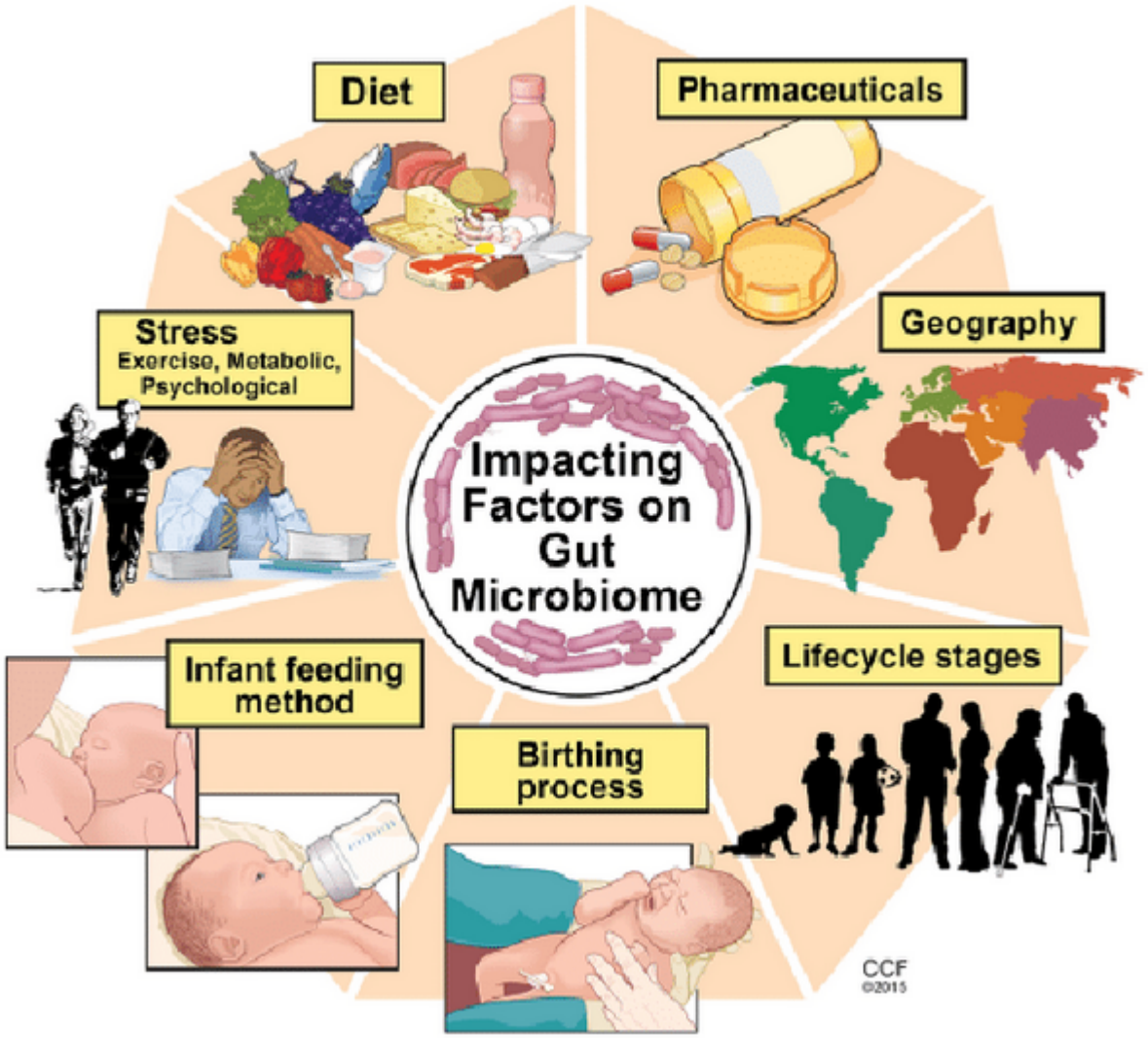




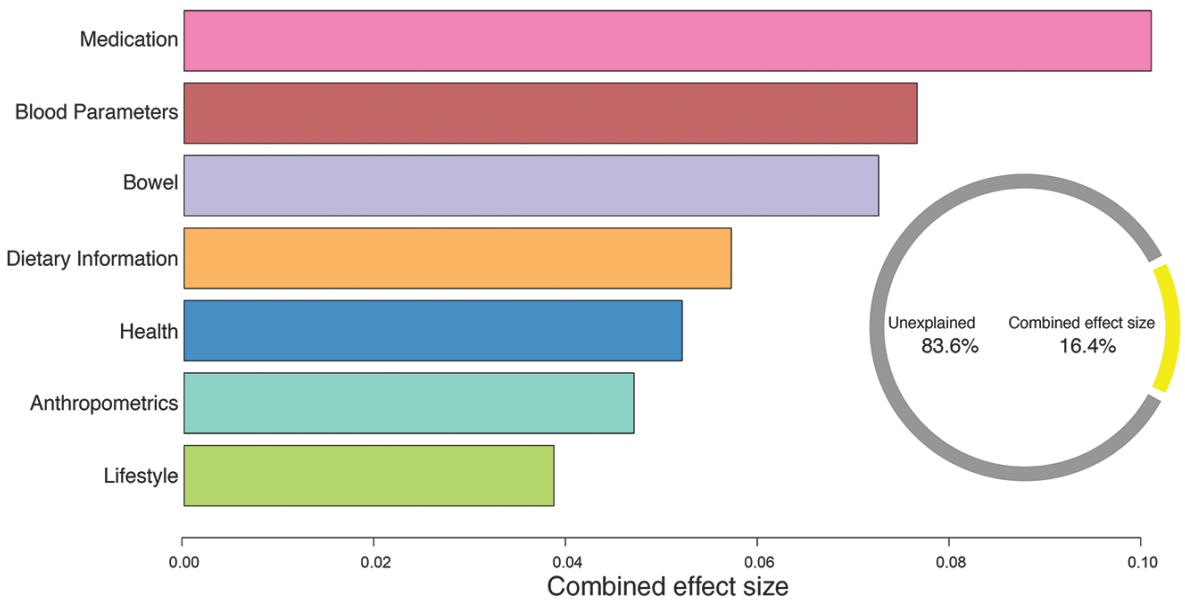
- 10 subjects tracked across 5-day animal- and plant-based diets.
- Animal-based diet increased bile-tolerant bacteria and decreased bacteria that metabolize dietary fiber.
- Bacterial metabolic activity tends to cluster by diet.
- Diet doesn't always overcome inter-individual differences in GMC structure (16S rRNA).

David et al, *Nature*, 505:559 2014

Numerous factors affect the gut microbiome



What explains gut microbiome variation within a population?



- Belgian Flemish Gut Flora Project (n=1106)
- 69 clinical and questionnaire-based covariates associated with microbiota compositional variation
- Stool consistency showed largest effect size and medication explained largest total variance.

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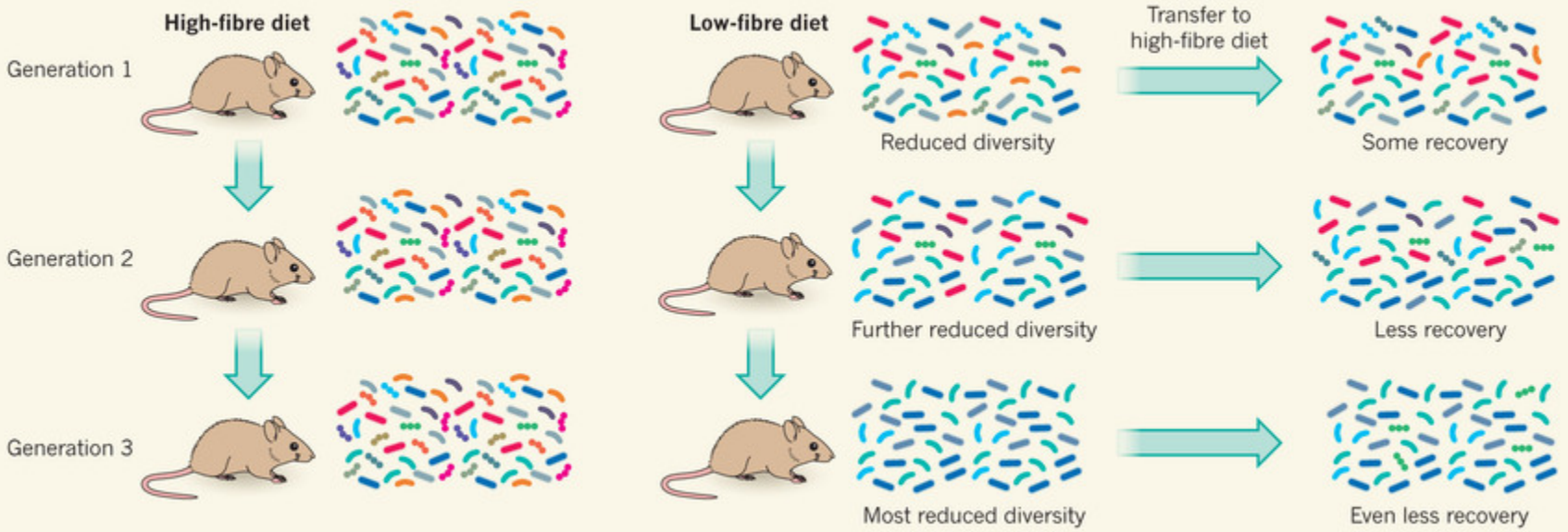
Falony et al. *Science* 352:560, 2016

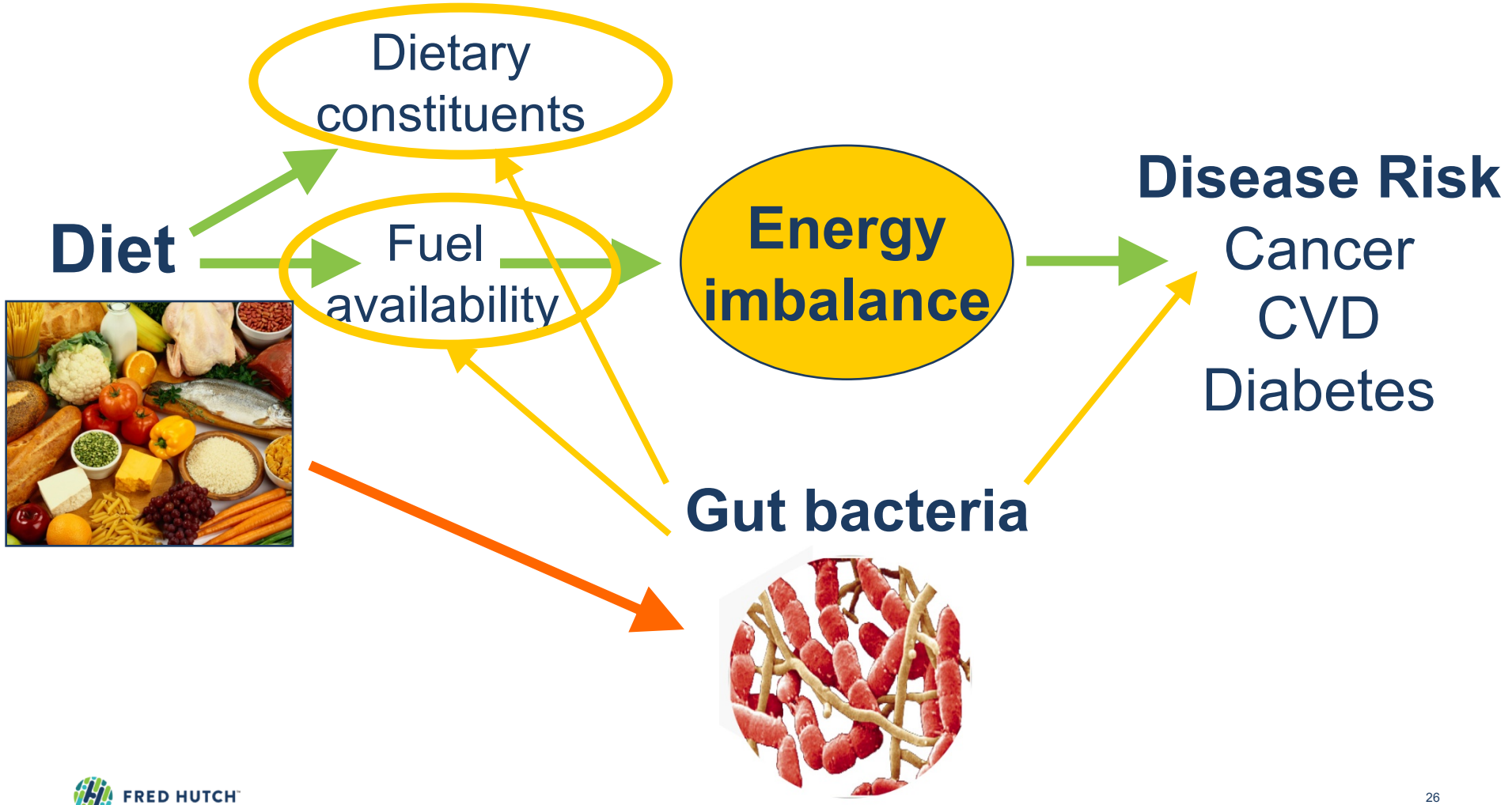
"They were my mother's microbes...
and now they're yours!"

Multigenerational Effects of Dietary Fiber on Bacterial Diversity



Martens E. *Nature* 529:158-159, 2016
Sonnenburg, E. et al. *Nature* 529: 212-215, 2016

Gut Microbial Effects on Diet and Human Health



How does the gut microbiome affect diet?

- Alters exposure to nutrients and bioactives
- Generates new compounds, that:
  - Serve as energy sources
  - Regulate metabolism
  - Cause or reduce inflammation
  - Cause or reduce oxidative stress
  - Are carcinogenic or chemoprotective

Bacteria Can Produce New Compounds from Dietary Constituents

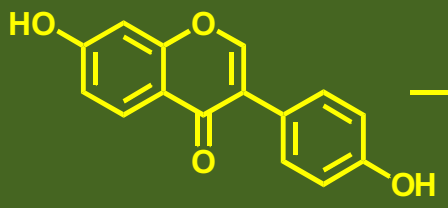
Food Component	Bacterial Metabolites
Dietary fiber	Butyrate and other SCFAs
Soy isoflavones	Equol, *O*-desmethylangolensin
Plant Lignans	Enterodiol, enterolactone
Ellagitannins	Urolithins A and B
Anthocyanins	Hippuric acid & small phenolics
Glucosinolates	Isothiocyanates



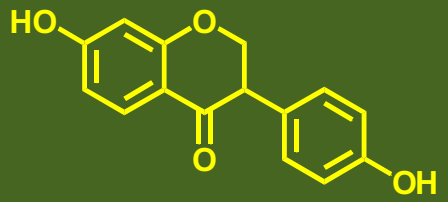




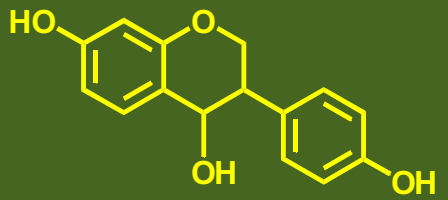
Microbial Production of Equol and ODMA From Soy Isoflavone Daidzein



Daidzein

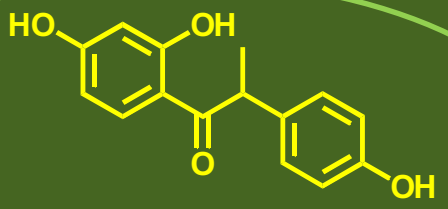


Dihydrodaidzein



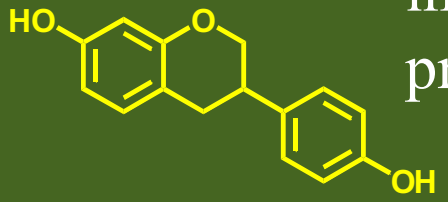
Cis/*Trans*-isoflavan-4-ol

80-90% of individuals produce



O-Desmethylangolensin

20-60% of individuals produce



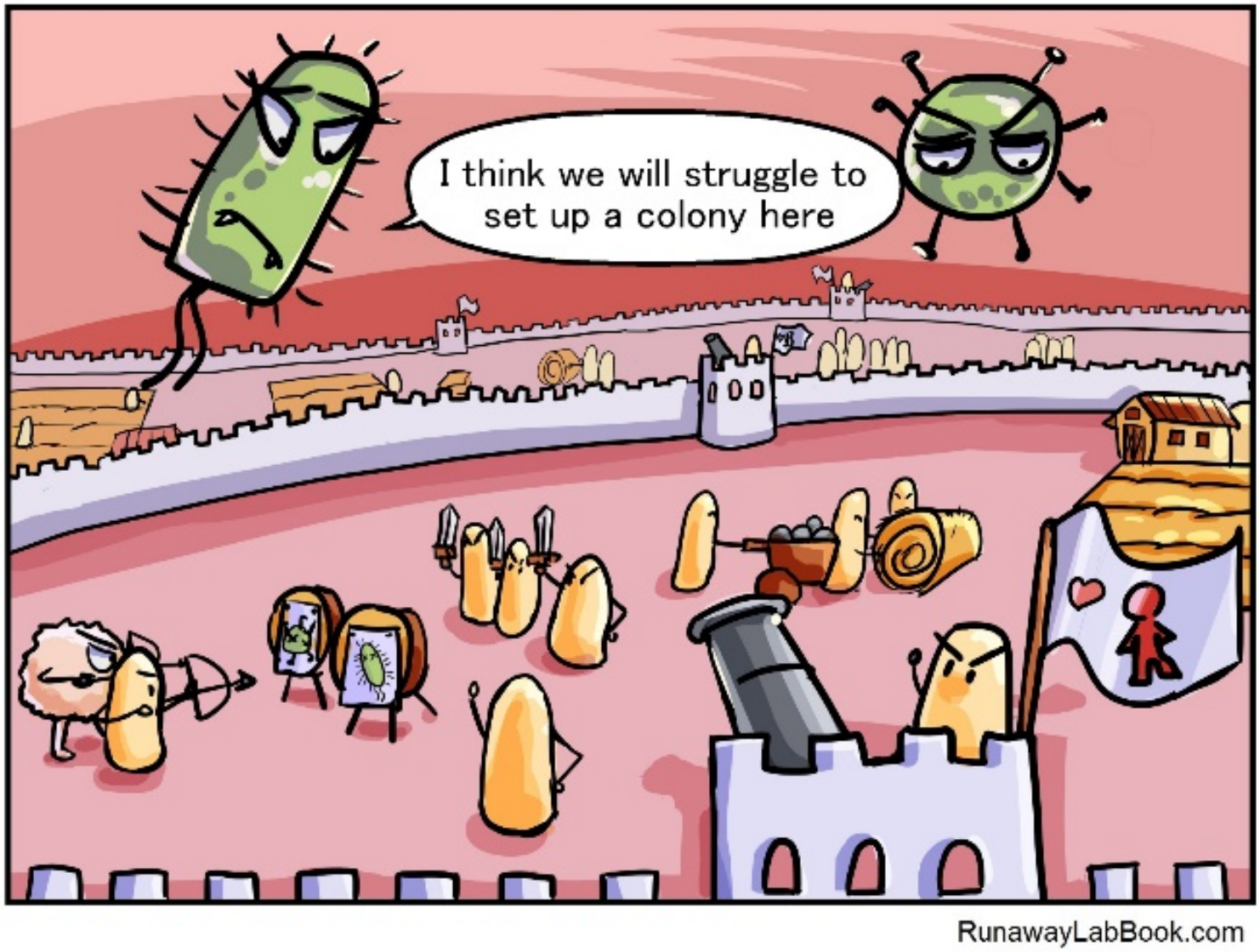
Equol

Daidzein-Metabolizing Phenotypes and Obesity and Cardiovascular Risk

- Equol producers, compared to nonproducers, had:
  - Higher fat-free mass
  - Lower blood pressure
  - Lower serum triglyceride), hs-CRP
  - O-DMA producers, compared to nonproducers, had:
  - Lower BMI and %body fat
  - Lower total cholesterol
- Habitual soy isoflavone intake had little relation to risk factors.

Liu Z-m, PLoS ONE 9(2): e87861, 2014.
Frankenfeld *et al., Eur J Clin Nutr,* 2014

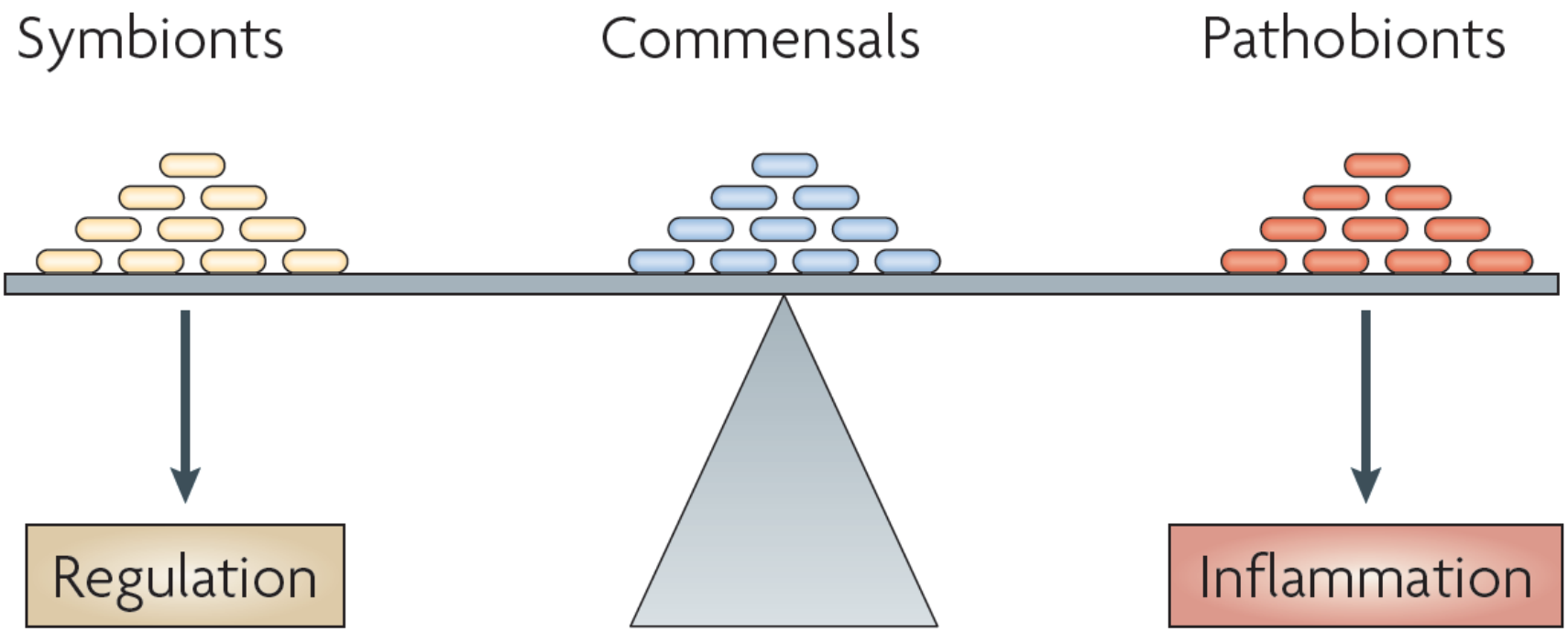
In a healthy gut microbial community, it is difficult to get new microbes to colonize.



Microbiome in Health and Disease

Eubiosis: Balance

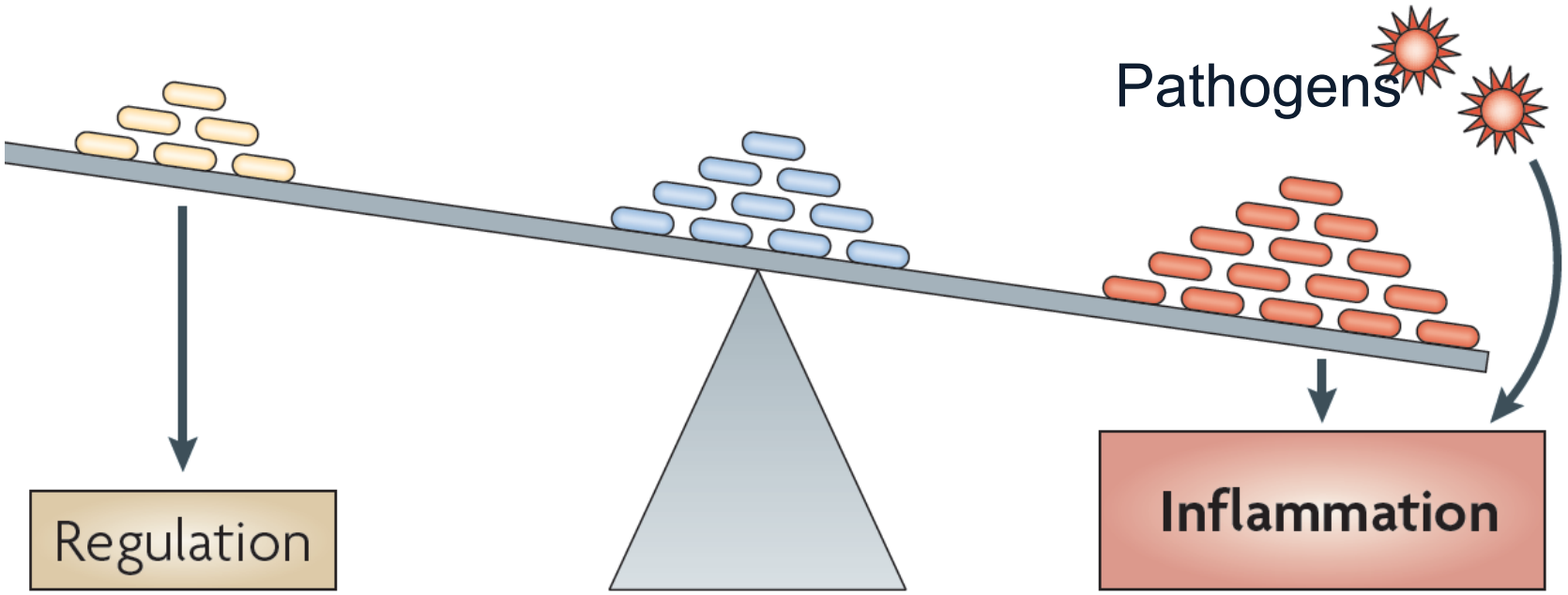
- Community of commensal, symbiotic, and pathogenic microoganisms in balance.



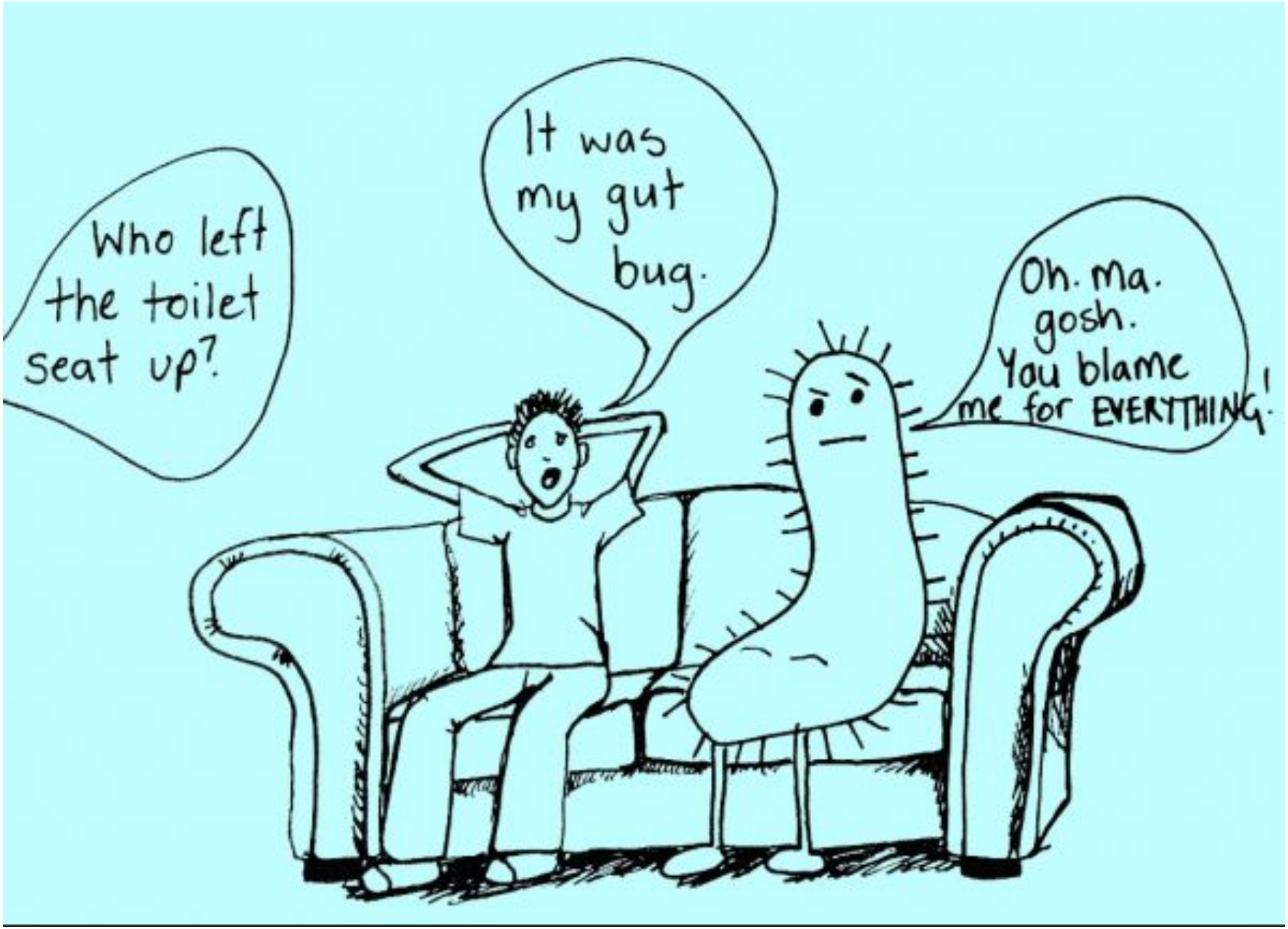
Round and Mazmanian, *Nat Rev Immunol*, 2010

Dysbiosis

- Aberrant microbiota profiles and/or metabolite alteration characterized by loss of metabolic homeostasis and increased inflammation.



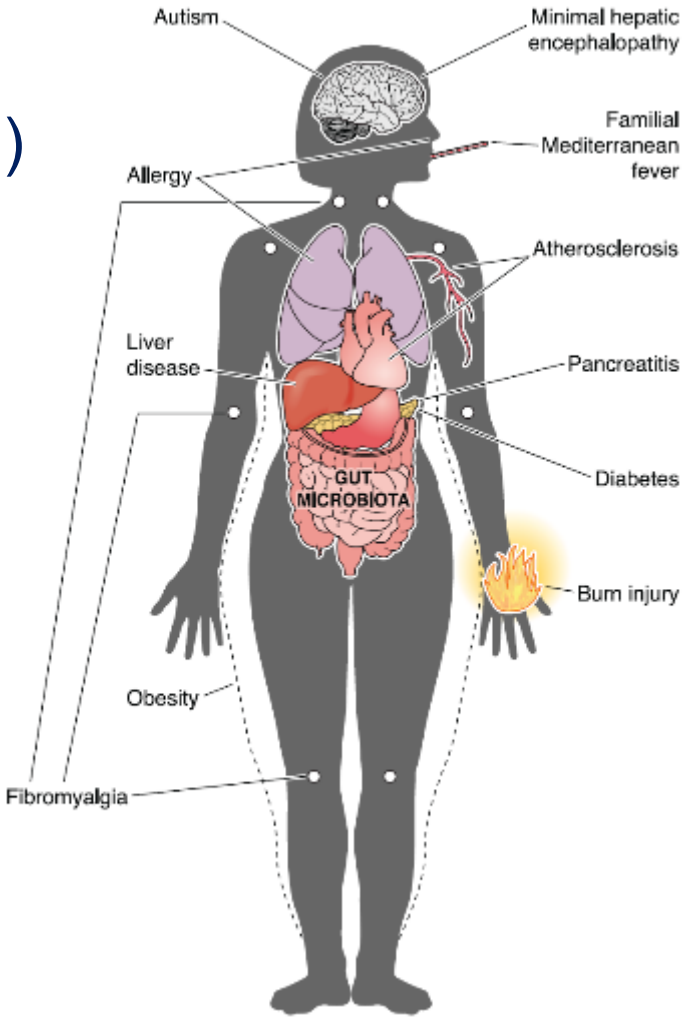
Round and Mazmanian, *Nat Rev Immunol*, 2010


Who left the toilet seat up?
It was my gut bug.
Oh. ma. gosh. You blame me for EVERYTHING!

Microbiome Dysbiosis and Disease

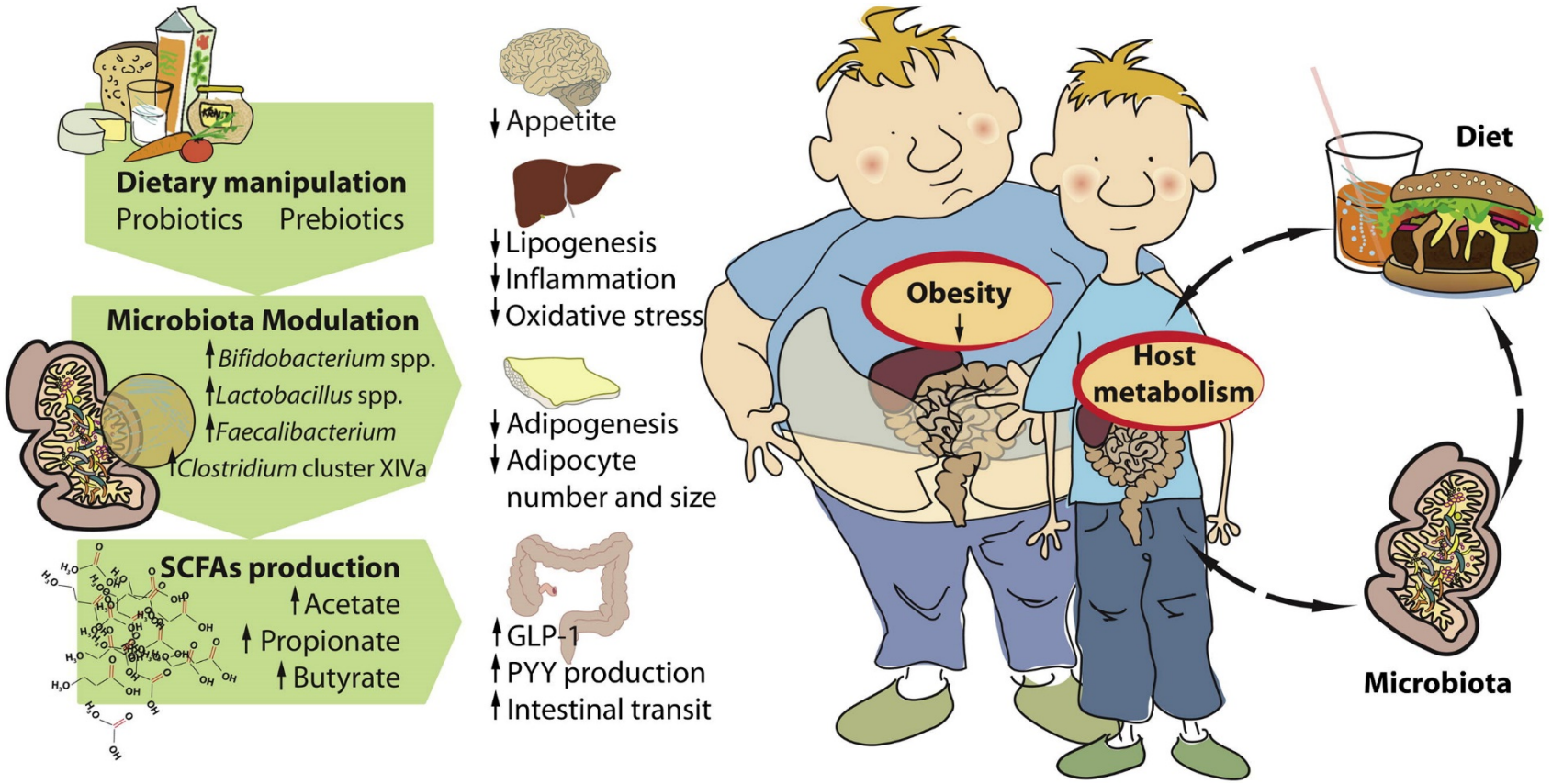
- Irritable Bowel Syndrome (IBS)
- Inflammatory Bowel Disease (IBD)
- Colon cancer
- Obesity
- Diabetes
- Metabolic syndrome
- Non-alcoholic fatty liver disease
- Heart disease
- Autoimmune disease
- Asthma

- Gut-brain axis



Sekirov I et al, *Physiol Rev*, 2010

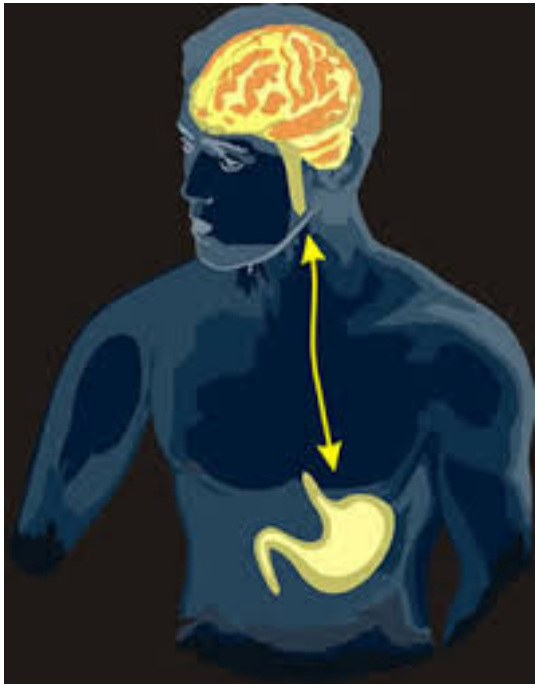
Diet and Gut Microbiome Affect Host Metabolism



Kovatcheva-Datchary & Arora, *Best Practice & Res Clin Gastroenterol*, 2013

Gut-Brain Axis

- Regulating satiety and whole body energy balance
- Regulating brain development
- Neurologic diseases
  - Autism
  - Depression
  - Dementia
  - Mood
  - Sleep patterns



Summary

- Diet influences the gut microbiome and its impact on the host.
- Gut microbiome is modifiable with diet.
- Need to consider the totality of gut microbial community.
- A large proportion of the inter-individual variation in the gut microbiome remains unexplained.
- Substantial work to be done to establish evidence to support causal relationships between the gut microbiome and health and disease.

QUESTIONS?

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“Everything is dandy—and our intestinal biomes are joyous.”