Gut Health and Diet of Older Adults

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Course Objectives

- Objective 1: Identify the role of the gut microbiota and factors that influence it through the lifespan.
- Objective 2: Identify how gut health influences disease states.
- Objective 3: Recommend diet change to promote a healthy gut.

What is the Human Microbiome?

- Microbe: tiny living organism, such as bacterium, fungus, protozoan, or virus

- Microbiome: collectively all the microbes in the human body; a community of microbes
  - Found on skin, nose, mouth, urogenital tract, GI tract
  - Up to 10x more microbial cells than human cells

- Gut Microbiota: the microorganisms living inside the GI tract
  - “Gut flora”
  - ~100 trillion organisms

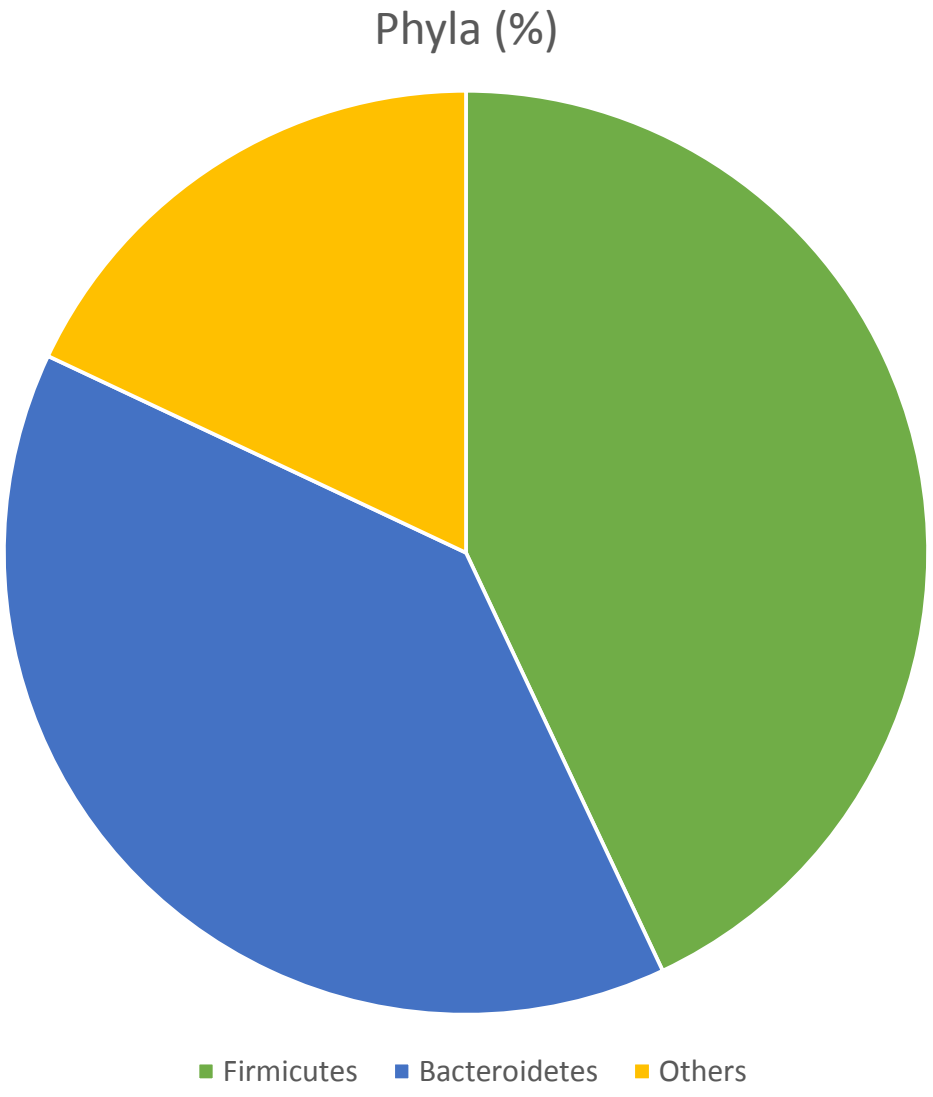
- Dysbiosis: change in the normal bacterial ecology; bacterial imbalance

What do Microbes do for You?

- Essential to maintaining our health
- Provide ability to harvest nutrients
  - 1’ by breaking down soluble fiber
- Produce energy otherwise inaccessible to the host
- Produce vitamins
- Prevent colonization by pathogens
- Help develop the immune system
- Metabolize carcinogens

Bacterial Phyla

- Estimated that 500 to 1,000 species of bacteria live in the human gut but belong to just a few phyla:
- Firmicutes and Bacteroidetes dominate but there are also Proteobacteria, Verrumicrobia, Actinobacteria, Fusobacteria and Cyanobacteria.



Microbiome Influences 4 Areas of Health

Nutrition	• Breaks down complex molecules of food • Influences cravings and satiety
Immunity	• Develop our adaptive immunity at birth • Allergies and/or autoimmune conditions can develop when early microbial exposures are disturbed
Behavior	• Gut-brain axis • Link between gut microbiome and brain disorders
Disease	• Intestinal overgrowth • Link between gut microbiome and disease states • IBD, Obesity, Diabetes, CVD, Parkinson's

Where does it start?

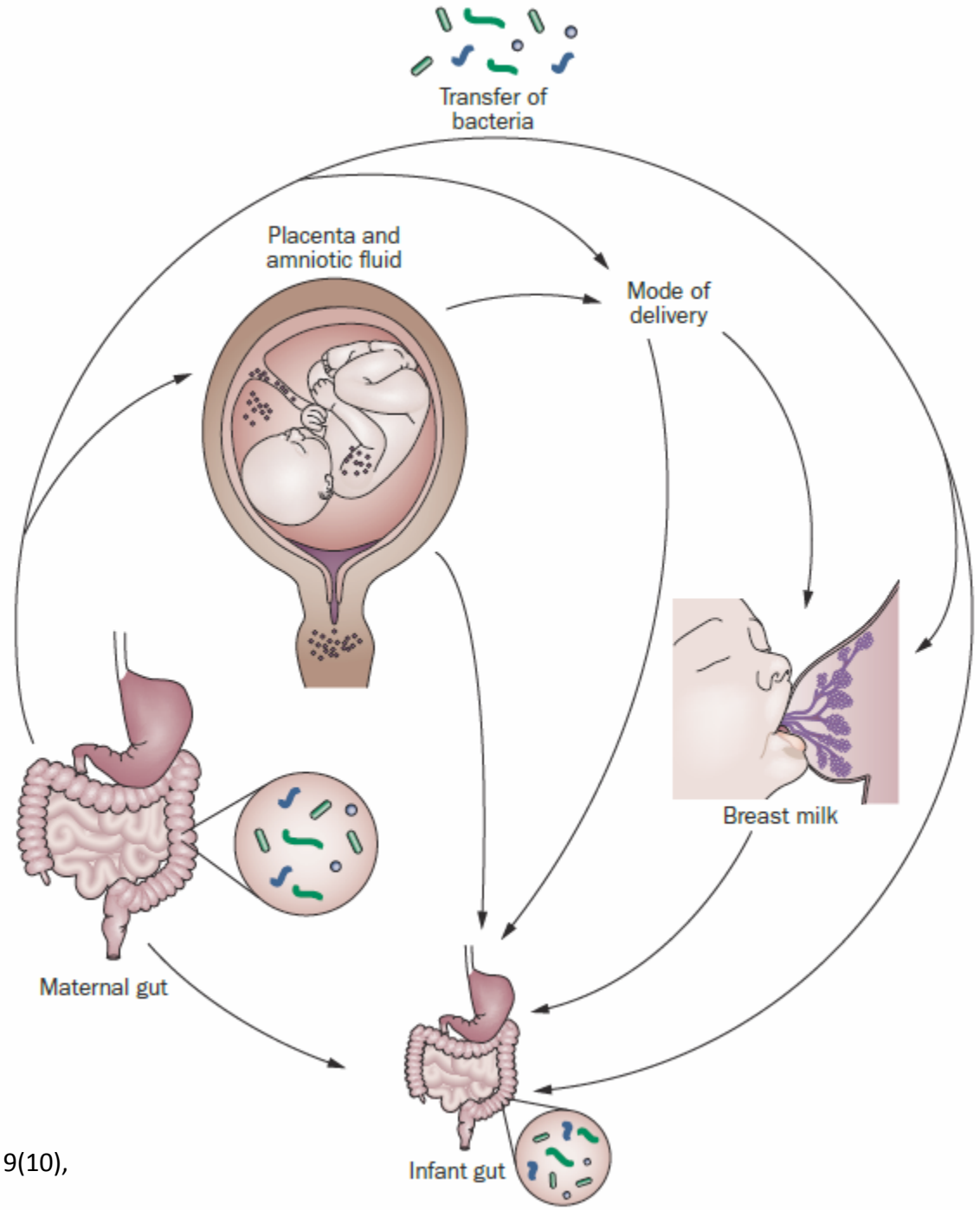
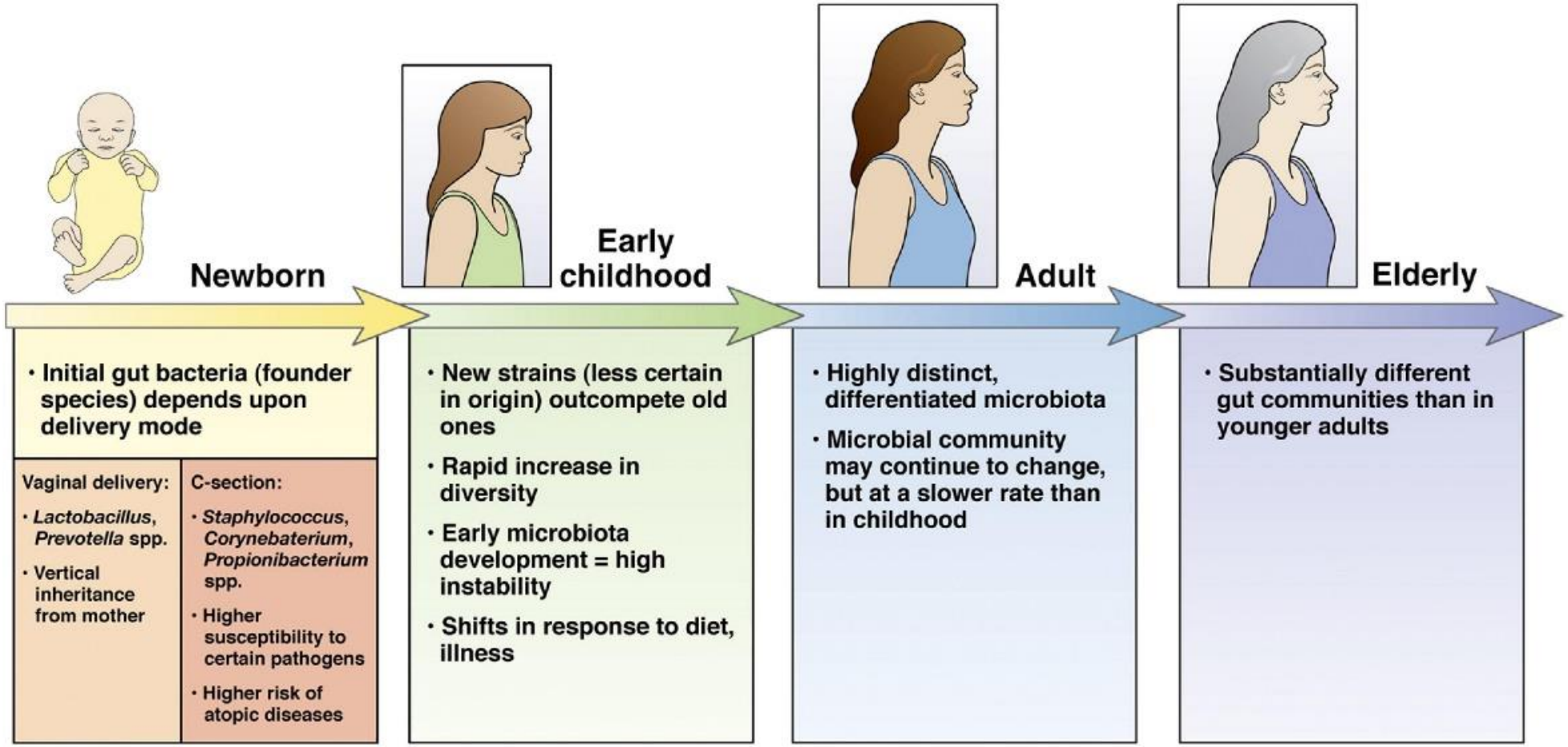


Figure 1 | The gut microbiota programmes host health—from mother to infant. The fetus comes into contact with microbes originating in the maternal gut through the placenta and amniotic fluid. A massive inoculum of maternal bacteria is encountered during vaginal delivery, which is also associated with increased maternal intestinal permeability and translocation of gut bacteria into breast milk. Breastfeeding not only modulates neonatal bacterial colonization and immune maturation, but is a direct source of maternal bacteria. After birth, skin-to-skin contact and nursing ensures direct transfer of maternal bacteria to the infant to enhance healthy immune and metabolic maturation.

Rautava, S., Luoto, R., Salminen, S., & Isolauri, E. (2012). Microbial contact during pregnancy, intestinal colonization and human disease. Nature Reviews. Gastroenterology & Hepatology, 9(10), 565. doi:10.1038/nrgastro.2012.144

Development of the Microbiota



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A Two-Sided Relationship

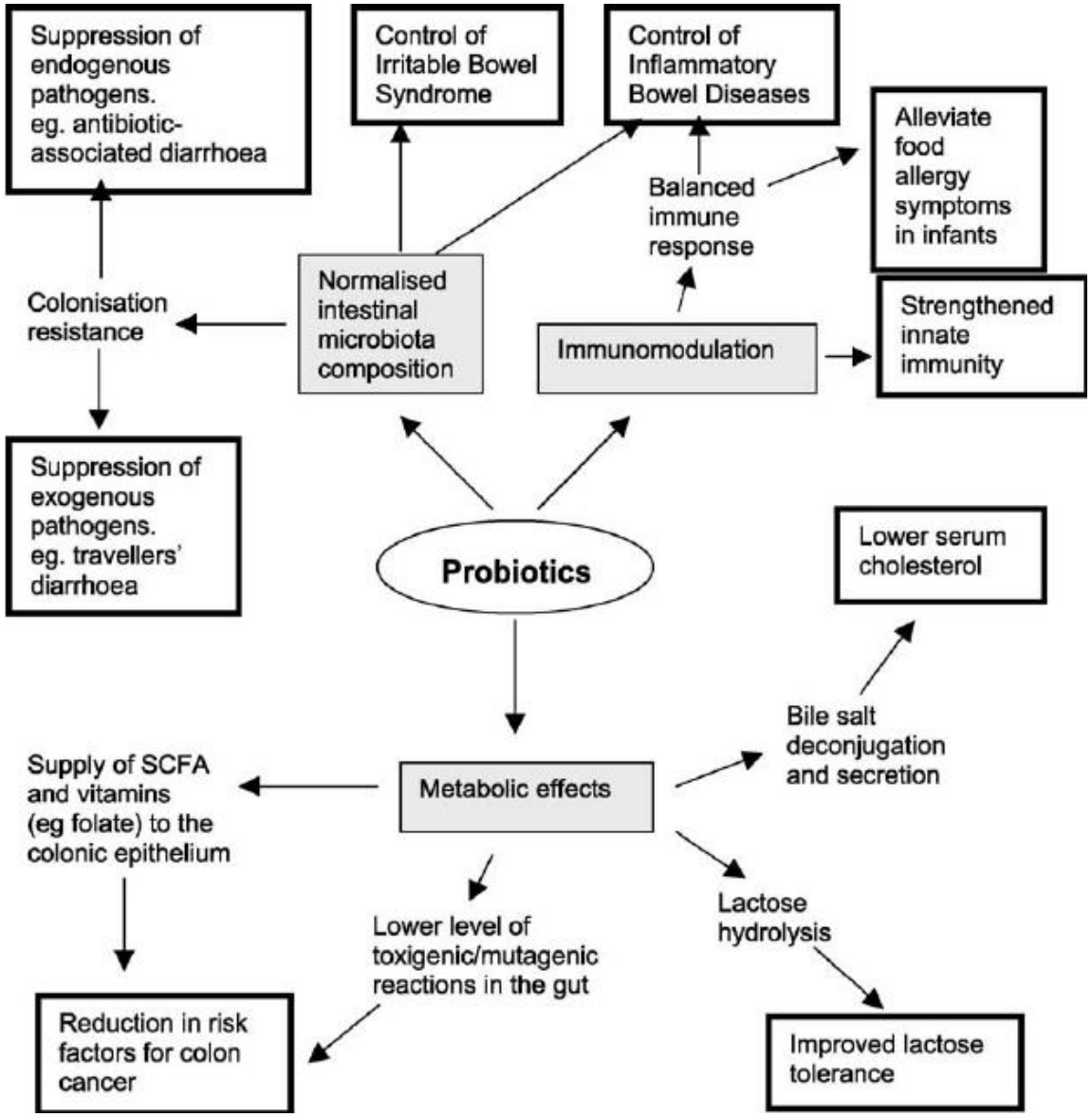
Dietary Component: Probiotics

- Probiotics
  - Foods or dietary supplements that contain live bacteria
  - WHO specifies that when administered in *adequate amounts*, confers a health benefit
- Prebiotics
  - Nondigestible food ingredient, which selectively stimulates the growth of gut bacteria
- Synbiotics
  - Combination of probiotics with a prebiotic

Dietary Component: Probiotics

- Probiotics can be formulated into many products
  - Food, meal replacement, dietary supplement, prescription drug
- Examples:
  - Lactobacillus
  - Yeast
  - Bifidobacterium
  - E. Coli
  - Bacillus

Probiotics: Proposed Health Benefits



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Probiotics: Conclusions

What We Don't Know

- How much we're eating/taking
  - Not required to be listed on packages
- How much live bacteria is available at the end of the product's shelf-life
- Which bacteria are helpful– not all have the same effect
- How much should be taken
- Who would most likely benefit from taking

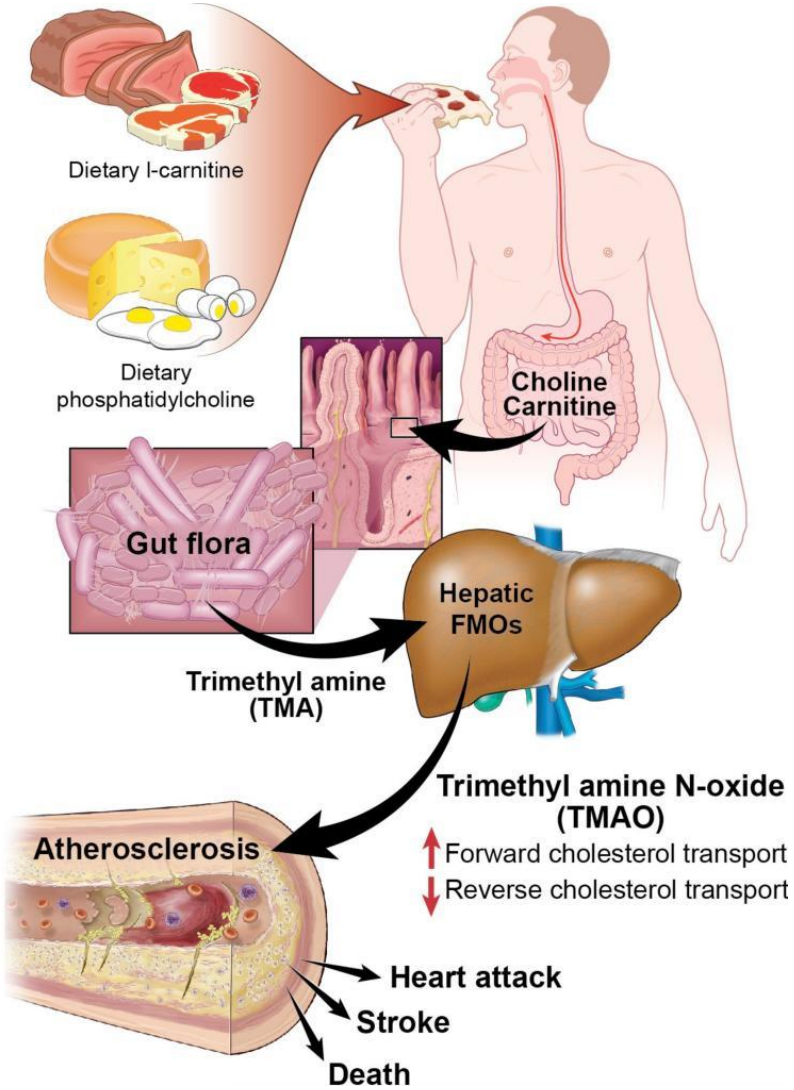
Probiotics: Conclusions

What We Know:

- Some probiotics are helpful
- The FDA has not approved any probiotics for prevention or treatment of any health ailments
- Supplements are most beneficial when containing at least 1 billion live cells/gram
- Supplements *probably* best if contain more than 1 type/strain of bacteria
- May be dangerous in those with weakened immune systems

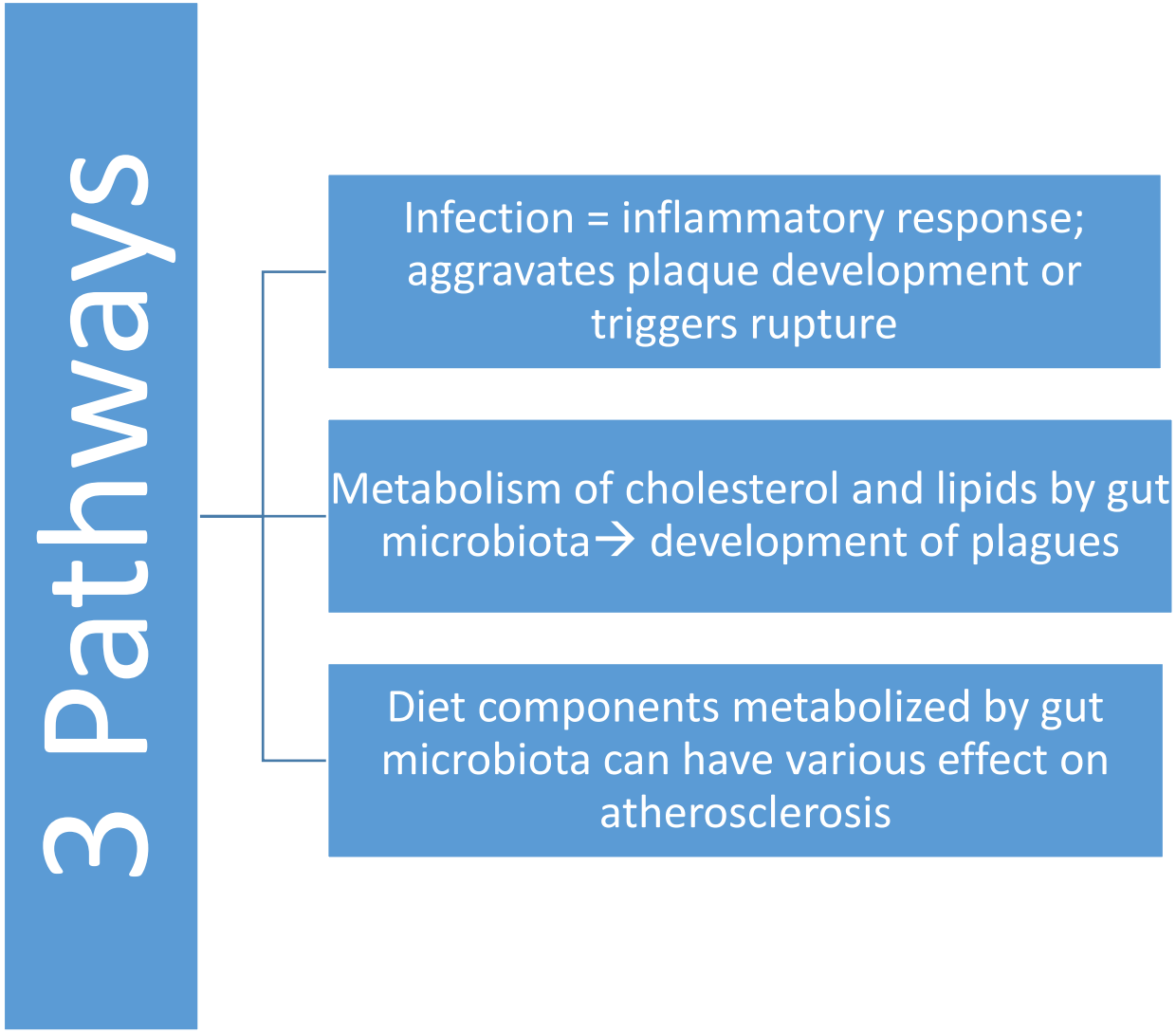
Microbiome and Cardiovascular Disease

- Dysbiosis can trigger systemic inflammation
- Trimethylamine N-oxide (TMAO)
  - Derived from gut microbiota as metabolites of dietary nutrients
  - ↑ TMAO = adverse CV events
- Elevated TMAO associated with poor outcomes for patient with heart failure and chronic kidney disease
- TMAO Foods



Brown JM, Hazen SL. Metaorganismal nutrient metabolism as a basis of cardiovascular disease. Curr Opin Lipidol. 2014;25:48–53.

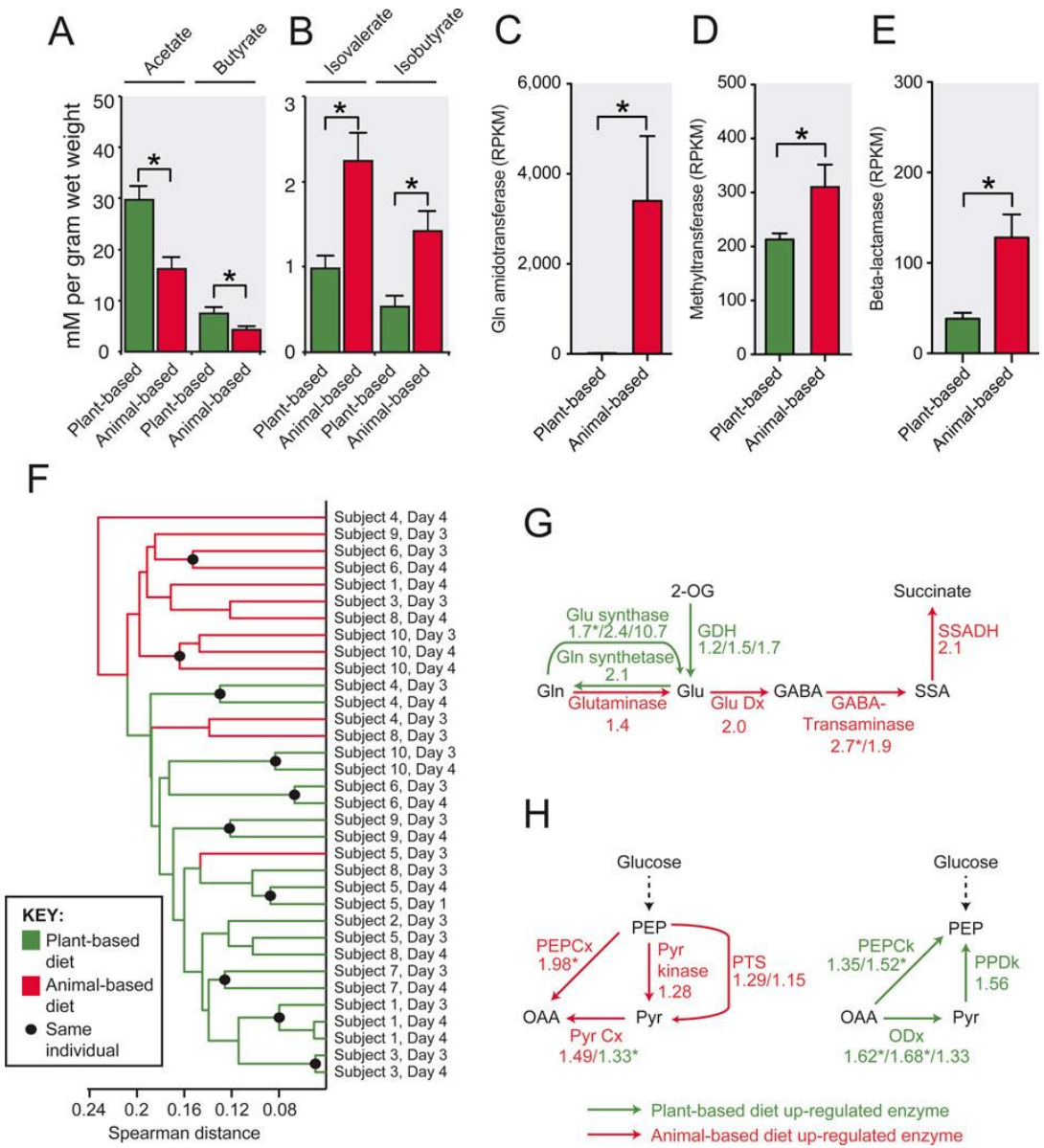
Microbiome and Cardiovascular Disease: Atherosclerosis



Microbiome and Cardiovascular Disease: Hypertension

- TMAO has role in regulation of arterial BP
- Very few human studies
- Short-chain fatty acids produced by microbiota influence BP that is related to renal sensory nerves

Evidence for the Mediterranean Diet



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Microbiome and IBD

- Ulcerative colitis & Crohns = chronic, relapsing inflammation
- Caused by dysbiosis?
  - Chicken or the egg scenario
- Not caused by a single microorganism
- Genetics, immunology, environmental factors & microbial all play a role
- BUT, inflammation does ↓ bacterial diversity and lowers the abundance of bacteriodetes and firmicutes

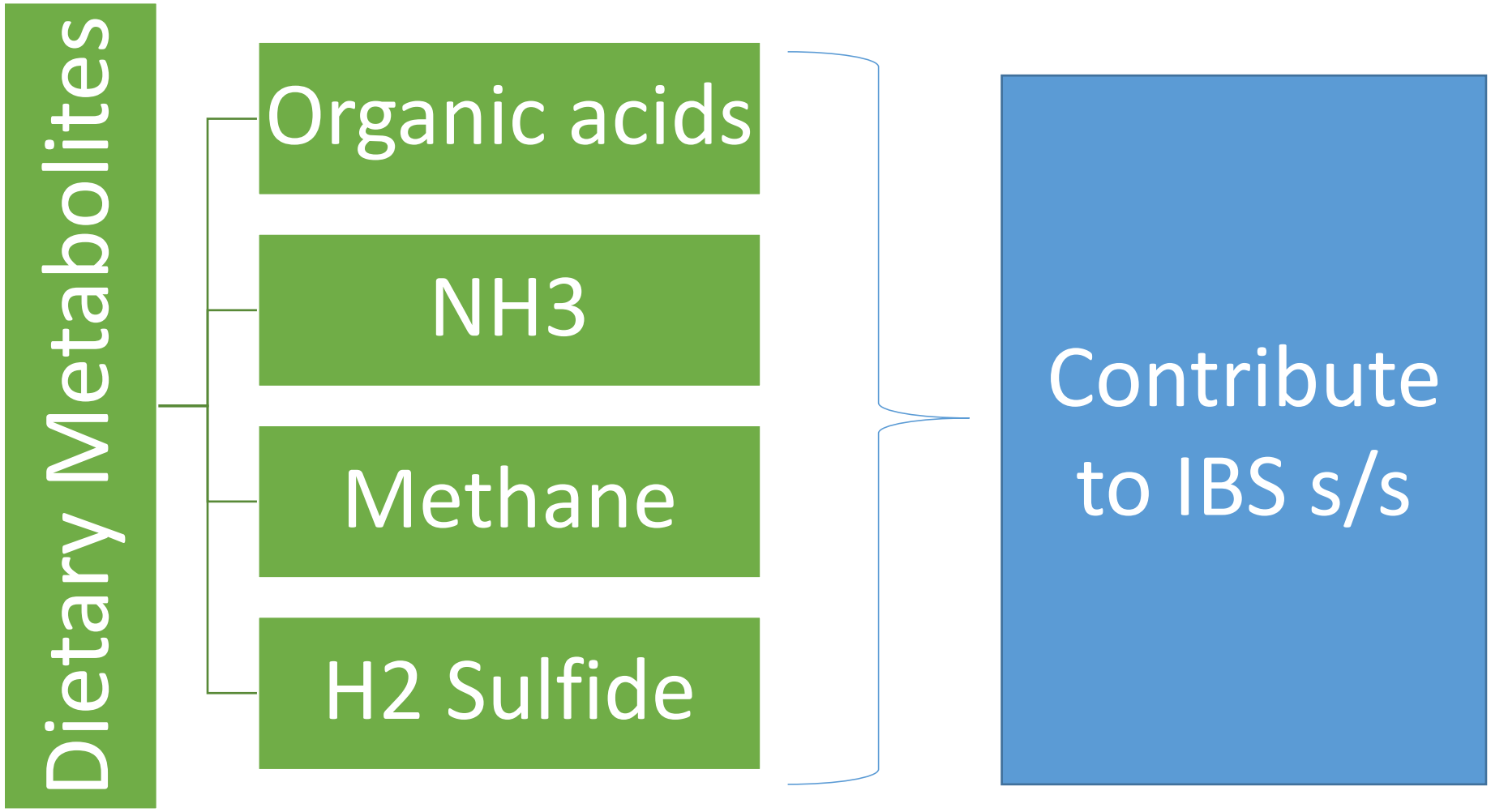
Ulcerative Colitis & Crohn’s

- Changed microbiota in UC and CD is a result of chronic inflammation
- Cycle of inflammation causing dysbiosis which causes limited short-chain fatty acids or anti-inflammatory signals & new inflammation

Microbiome and IBS

- Evidence of dysbiosis
  - Characterized by alterations in firmicutes and proteobacteria
  - Higher amounts of Dorea, Ruminococcus, haemophilus parainfluenzae
- Studies→ ~10% of IBS cases begin after an episode of gastroenteritis (PI-IBS)
- Factors known to precipitate or exacerbate IBS also induce intestinal dysbiosis
  - Antibiotic use
  - Enteric infection
  - Stress
  - Dietary factors

Microbiome and IBS: Dietary factors



Evidence for Dietary Fiber

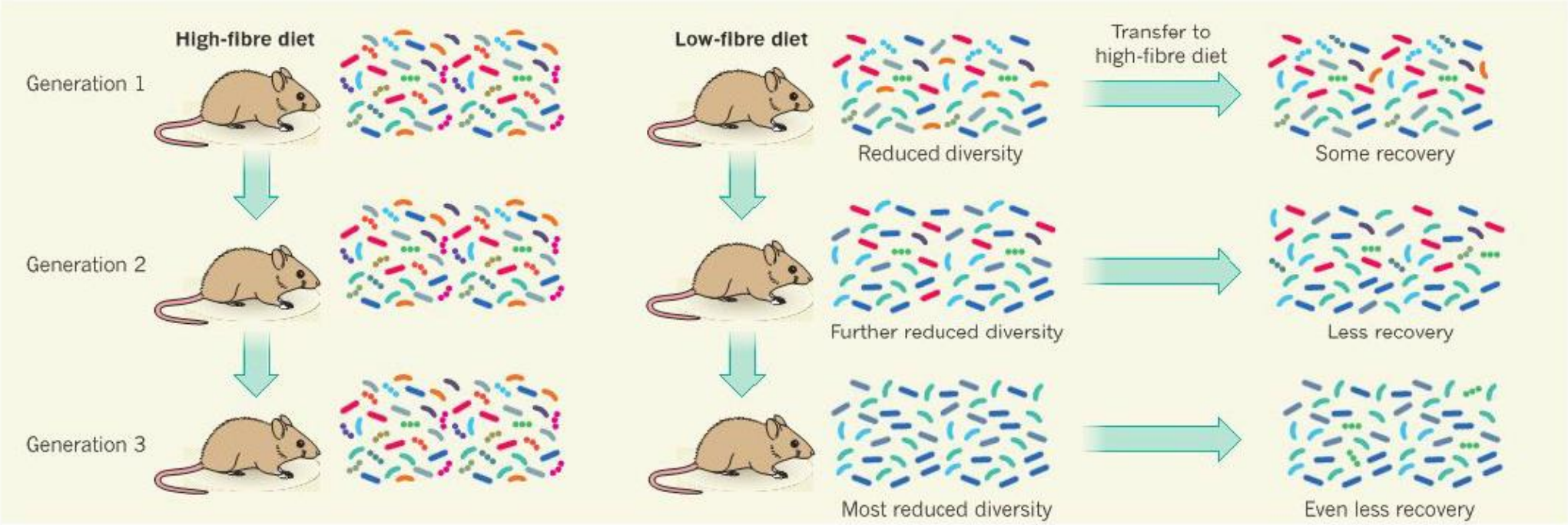


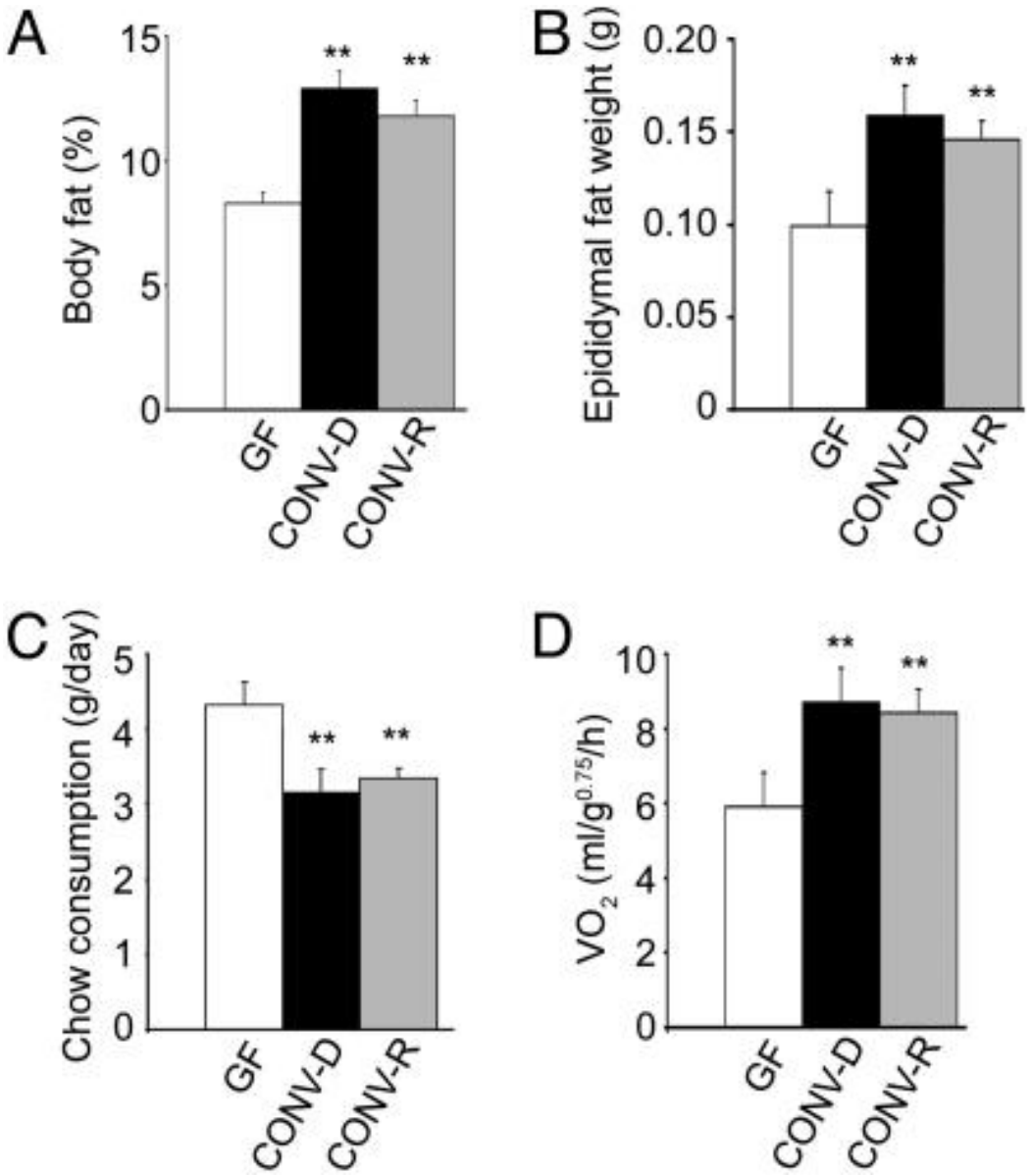
Figure 1 | Loss of diversity. Sonnenburg *et al.*[1] found that mice fed a low-fibre diet had a lower species diversity in their gut microbiota than mice fed a high-fibre diet. In first-generation mice, most (but not all) of this diversity was recoverable when mice on the low-fibre diet were switched to a high-fibre diet. However, the authors found that diversity loss was greater in each subsequent generation maintained on a low-fibre diet, and that the degree of recovery also decreased, implying extinction of some microbial species.

Martens, E. C. (2016). Microbiome: Fibre for the future. Nature, 529(7585), 158-159. doi:10.1038/529158a

Microbiome and Obesity

- Western diet = microbial dysbiosis
  - Changes in firmicutes/bacteroidete ratio
- Gut diversity differs in obese vs nonobese
- Gut microbiota influences gut permeability→ leads to entry of microbial lagans into the bloodstream→ ↑ insulin resistance & prevent peripheral uptake of fat
- Unlikely that obesity is caused by microbes… but diet has effect on microbiota

Microbiome and Obesity



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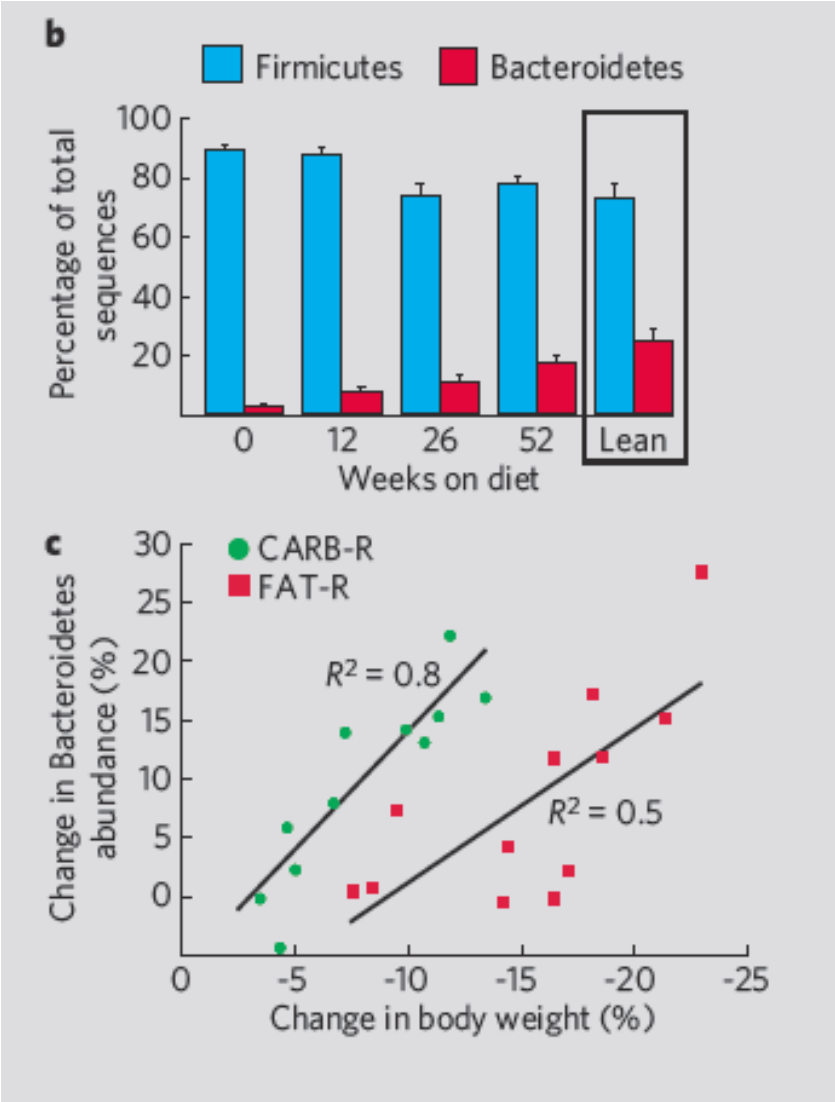
Microbiome and Obesity



- 12 obese individuals
- Randomly assigned to either a fat-restricted (FAT-R) or to a carbohydrate-restricted (CARB-R) low calorie diet.
- The composition of their gut microbiota was monitored over the course via stool samples
- Before diet therapy, obese people had fewer Bacteroidetes ($P<0.001$) and more Firmicutes ($P=0.002$) than did lean controls
- Over time, the relative abundance of Bacteroidetes increased ($P<0.001$) and the abundance of Firmicutes decreased ($P=0.002$), irrespective of diet type (Fig. 1b).
- Increased abundance of Bacteroidetes correlated with percentage loss of body weight, and not with changes in dietary calorie content over time

Type 2 Diabetes and Obesity

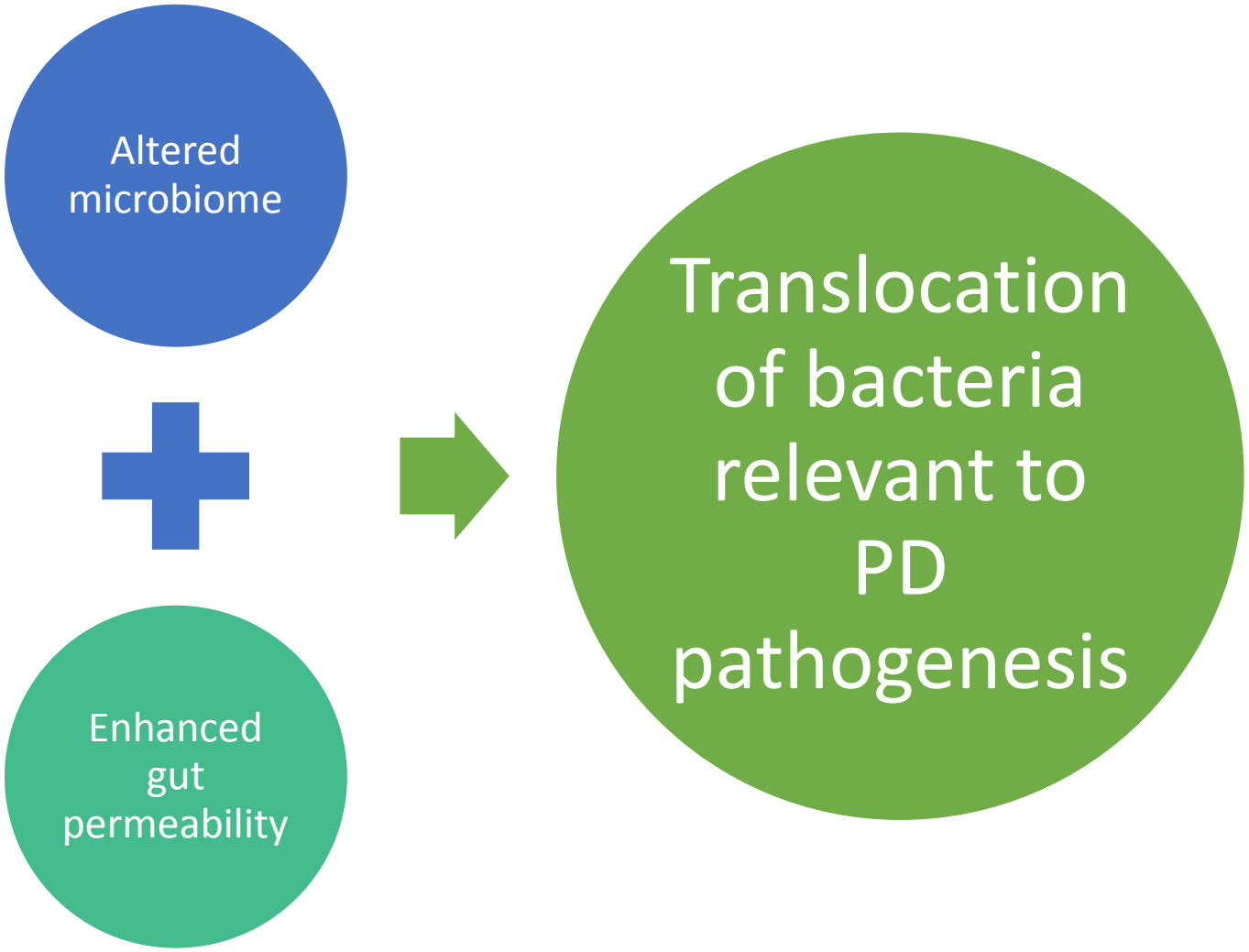
- Alterations in gut microbial populations have been linked to:
  - Changes in insulin sensitivity
  - Altered glucose metabolism
  - Development of metabolic syndrome

- In Type 2 DM: possible alterations in butyrate producing bacteria such as Faecalibacterium prausnitzii

Microbiome and Type 2 Diabetes Mellitus

- Potential mechanism underlying the role of gut microbe and Type 2 DM
  - Inflammation and intestinal permeability contribute to development
  - Lipopolysaccharides (LPSs) have a key role in development of inflammation and insulin resistance
  - Individuals with Type 2 DM have been shown to have ↑ inflammation and LPS levels
  - High-fat diet have been shown to ↑ LPS levels
  - More permeable gut allow more LPS to enter the circulation

Microbiome and Parkinson's Disease



- Modulation of the microbiota-gut-brain-axis through pharmabiotic intervention may be an upcoming therapy in PD

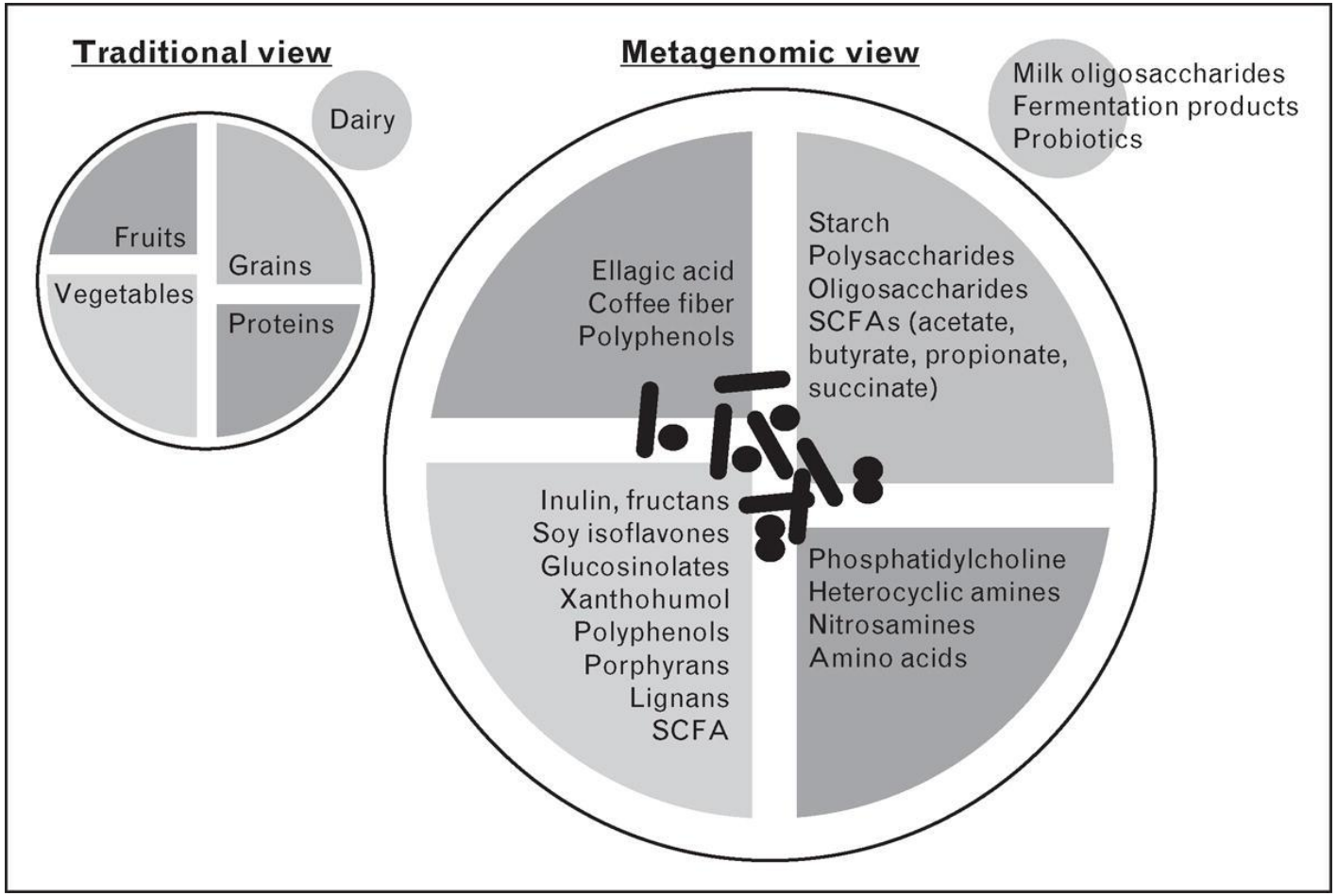
Microbiome and Parkinson’s Disease

- Matrix metalloproteinase-9 (MMP-9), a major component of the basement membrane, may contribute to the pathogenesis PD
- MMP-9 is associated with a loss of intestinal microbiota
- Consumption of probiotics may decrease MMP-9
- Consumption of plant based (Mediterranean) diet may decrease MMP-9

What can WE Do?

- Plant based or Mediterranean diet
- Initiation of probiotics
- High fiber diet
- Bariatric surgery
  - RYGB results in change in the ratio of bacteria
- Avoidance of emulsifiers & artificial sweeteners– remains unknown

‘Metagenomic’ View of Nutrition



- The human diet is vastly more complex than a simple combination of sugar, fat, and protein.
- The interactions between food-associated microbes and the gut microbiome need to be better characterized.

Dutton, R. J., & Turnbaugh, P. J. (2012). Taking a metagenomic view of human nutrition. Current Opinion in Clinical Nutrition and Metabolic Care, 15(5), 448-454. doi:10.1097/MCO.0b013e3283561133

The Future…

- The past has looked at what microbes exist
- The future looks to what the microbes are doing
- Microbiome research is an emerging science; as data increases, the number of disease linked to alterations in the gut will likely grow

References

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