





BiomeFX in Clinical Application: IBS-C

By Lacey Hall MS RD


Irritable Bowel Syndrome

- Most common functional GI disorder
 - IBS-Diarrhea, IBS-Constipation, or both
 - Pain, discomfort, gas, bloating, straining
 - 18- 40 year old patient population
 - Women are twice as likely to exhibit symptoms
 - Gut-brain interaction impacting peristalsis
 - Stress, nervousness, and anxiety linked to changes in motility
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Testing for Irritable Bowel Syndrome-C

- No lab test that can definitively diagnose IBS-C
 - Biofeedback assessment
 - Anorectal manometry to sense changes in volume and pain receptors
 - Post-infectious IBS-C
 - Antibodies to vinculin
 - Detection of cytolethal distending toxin B (CdtB)
 - Is stasis stemming from small intestine or colon?
 - MMC versus Peristalsis
 - Is it SIBO
 - Microorganism patterns in stool tests
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Most Common Conventional Treatments: IBS-C

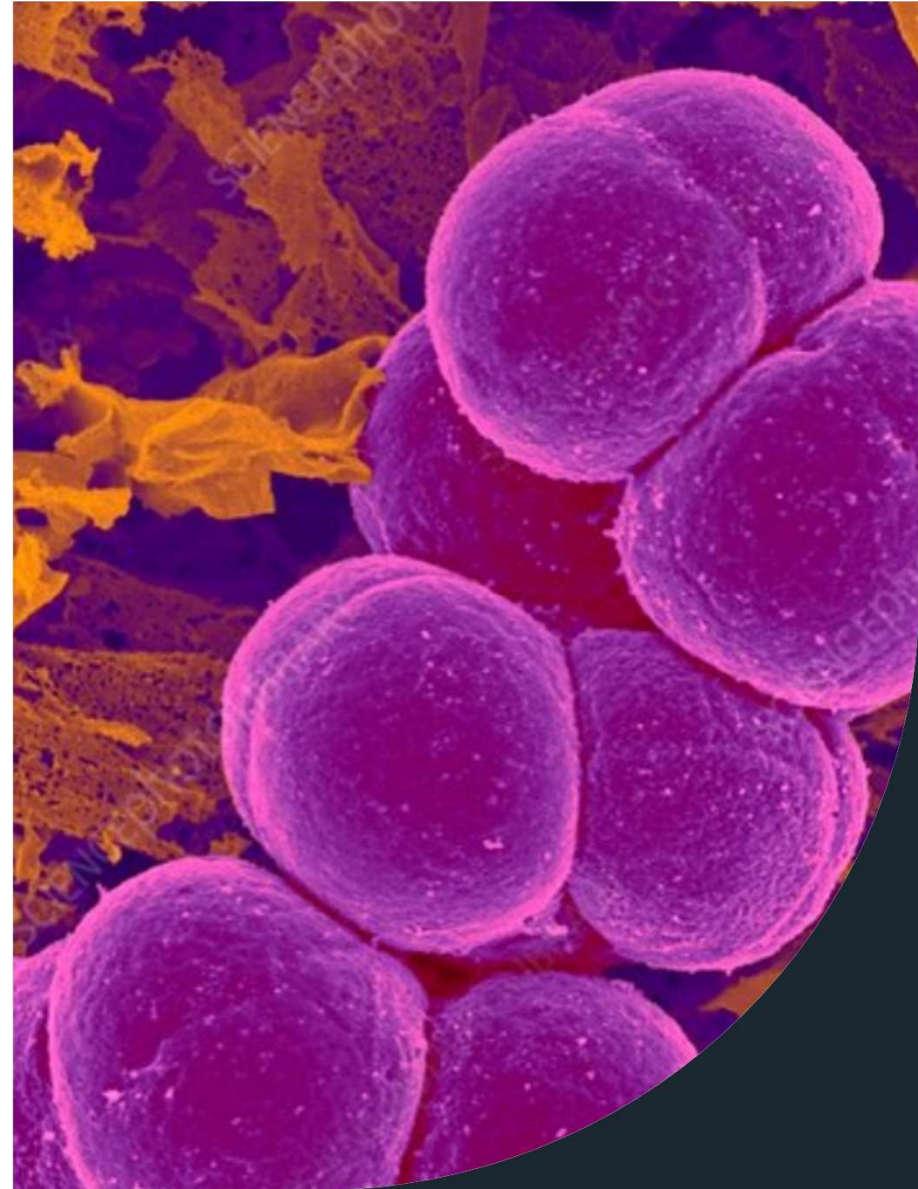
- Dietary
 - Increase fibre
 - Low FODMAP
 - Exercise
 - Laxatives
 - Pro-secretory agents
 - Probiotics
 - Antibiotics/antimicrobials
 - Cognitive Behaviour Therapy
 - Hypnotherapy
 - Antidepressant medication
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Consequences of untreated IBS-C

- Intestinal hyperpermeability
 - Chronic inflammation
 - LPS
 - TNF- α
 - TMAO
 - Autoimmunity and immune system dysregulation
 - Altered enteric and central neuronal activity
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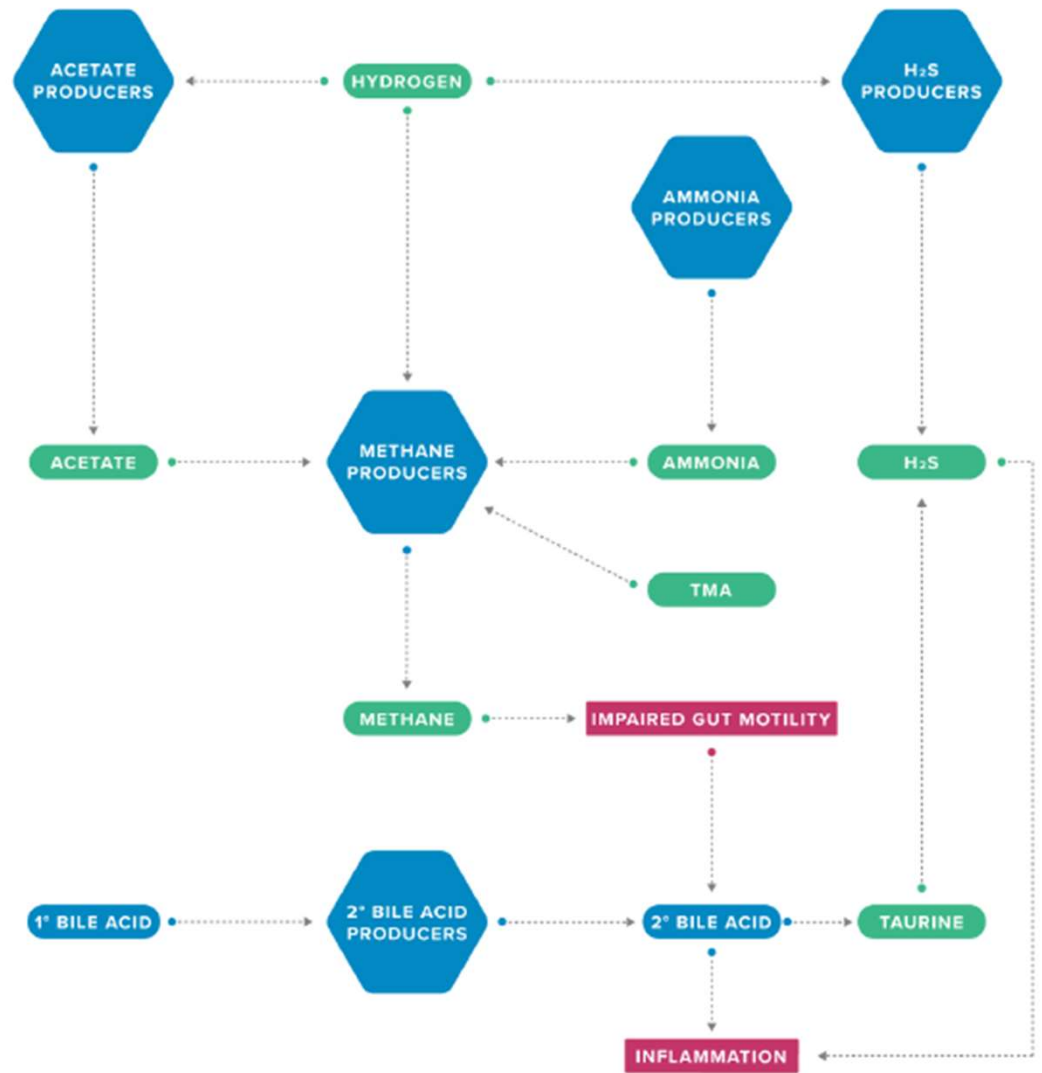
Archaea

- Single-cells prokaryotic organisms
- Not bacteria
- Euryarchaeota and methanobacter species reside within this domain
- Secrete methane gas CH₄
- Methane cannot be utilized by human cells
 - Bloating, gas, slowed transit, weight gain
- Prefer a slightly neutral intestinal pH

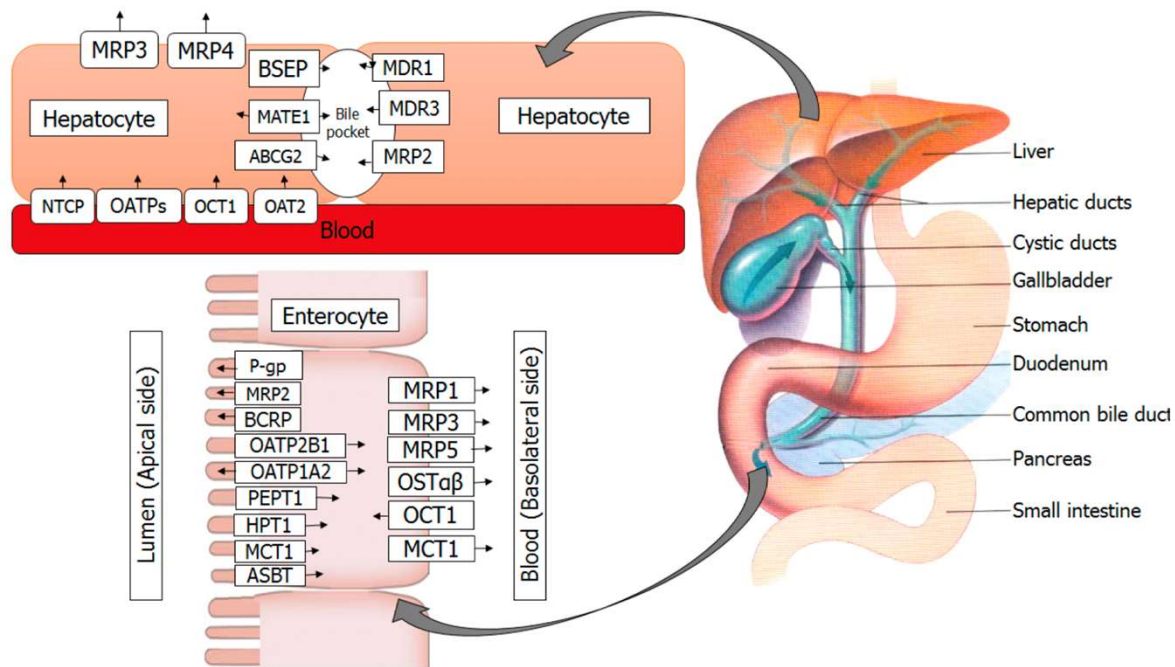


Methanogens

- Can feed off many substrates
 - Hydrogen
 - Acetate
 - Ammonia
 - TMA
- Block the conversion of acetate to butyrate (gut-brain!)
- Dysfunctional phase 2.5 and phase 3 detoxification pathways
- Linked to inflammation



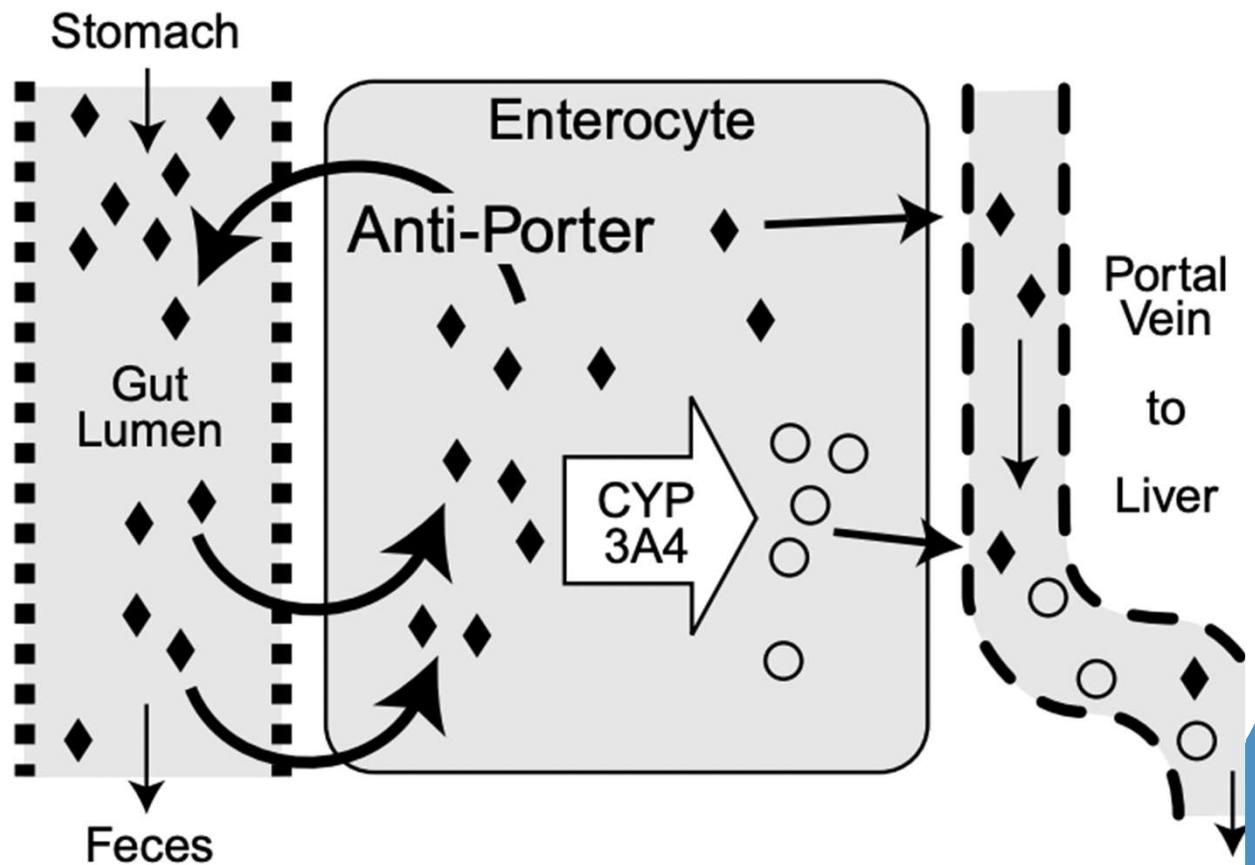
Phase 2.5 Detox: Anti-Porter System (P-Glycoprotein)



- 350 Anti-porter proteins
- P-Glycoprotein most studied (P-gp)
- Located in small intestine (on microvilli), liver, kidney, BBB
- Efflux pumps work to push toxins out of cells
- Can help or hinder Phase 1 detoxification
- Constipation can downregulate p-glycoprotein expression

Phase 2.5 Detox: Anti-Porter System (P-Glycoprotein)

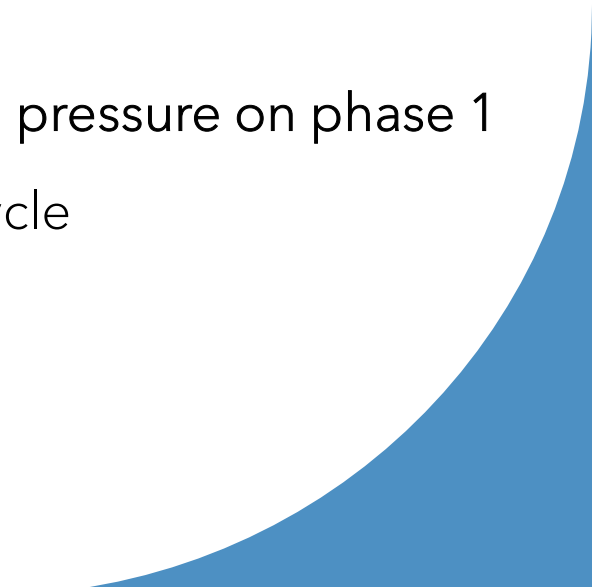
- Butyrate and secondary bile acids promote more anti-porters in the intestinal lumen
- *Bacillus* and *Clostridia* species shown to **induce** the most p-glycoproteins in the gut
- Lipopolysaccharide (LPS) from inflammatory bacteria and **methane** inhibit p-glycoprotein expression
- Low p-gp associated with IBD, UC, cancers



Phase 3 Detoxification: Excretion and Waste Removal

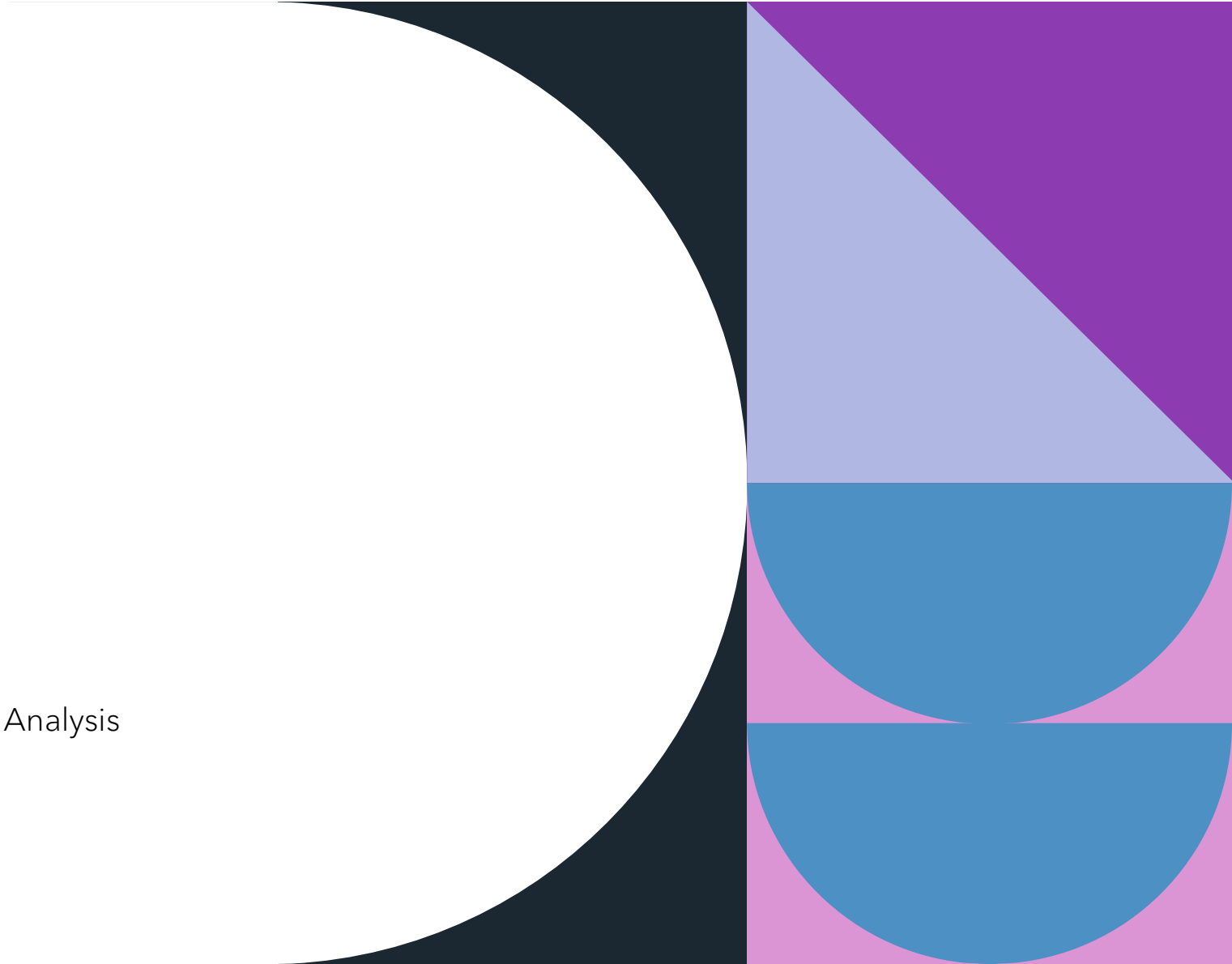
- Conjugated metabolites move through bile into the intestinal lumen
- A healthy gut is imperative to phase 3
- Dysbiosis from LPS can shut down phase 2.5 and can deconjugate metabolites from phase 2

This can cause toxins to re-enter the blood stream, putting pressure on phase 1

- Deconjugation of metabolites restarts the detoxification cycle
 - If you're not pooping, you're not detoxifying properly
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BiomeFX

Function Microbiome Analysis

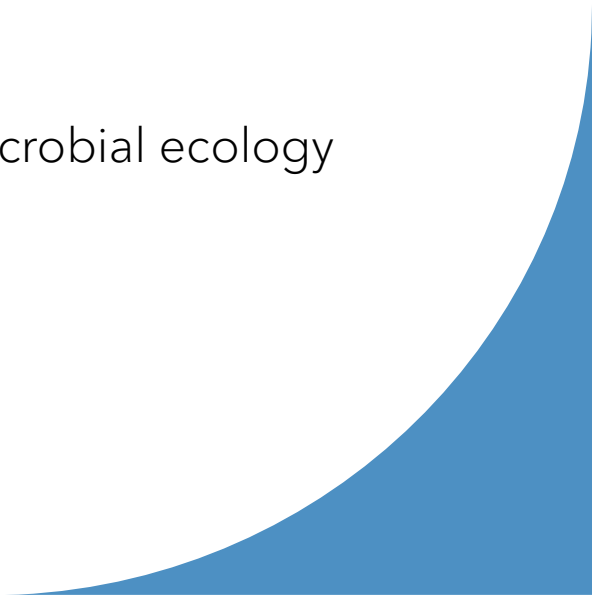


What is BiomeFX

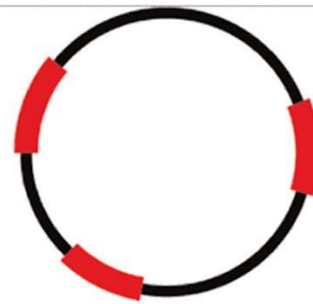
- 21-page report
- Shotgun metagenomic sequencing (whole genome sequencing)
- Indices; 3
- Dysbiosis Ratios: 3
- Phylum: 15
- Families: 25
- Pathogens: 34
- Keystone Species: 12
- 86 total bacteria/groups
- Functions: 25 functional measurements
- Sample report at www.biomefx.com
- 30 and 60 minute consultations



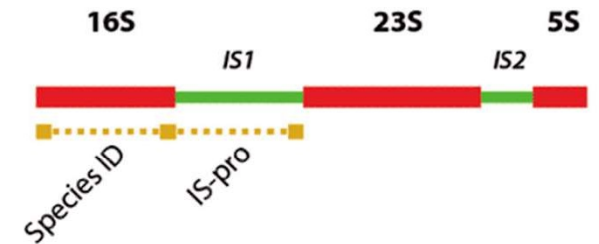
BiomeFx...What You Will Learn

1. *Who* is in the gut
 2. *What* they are doing there
 3. If who is there are in *balance*
 4. How to *restore* balance, strength and resiliency of the microbial ecology
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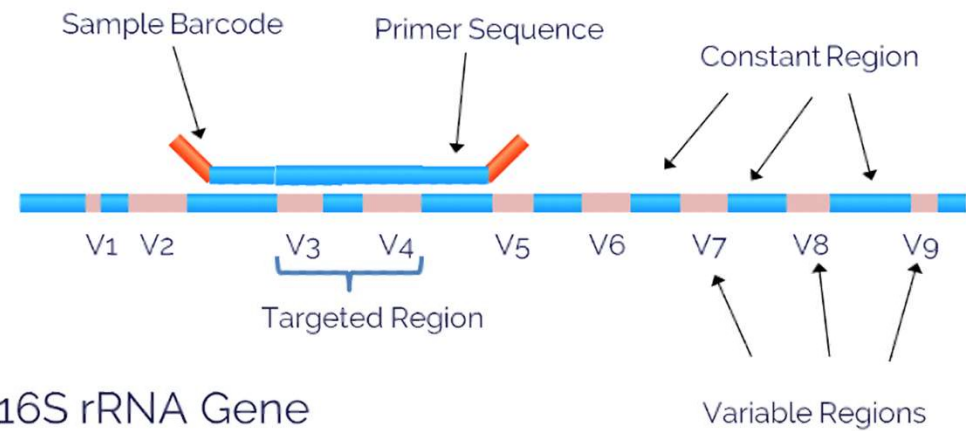
16s rRNA Sequencing



○ Bacterial chromosome
■ Ribosomal DNA



■ Ribosomal DNA (sequence important)
■ Interspace DNA (length important)



16S rRNA Gene

Whole Genome Sequencing

End-to-end sequencing of DNA

Strain-level specificity

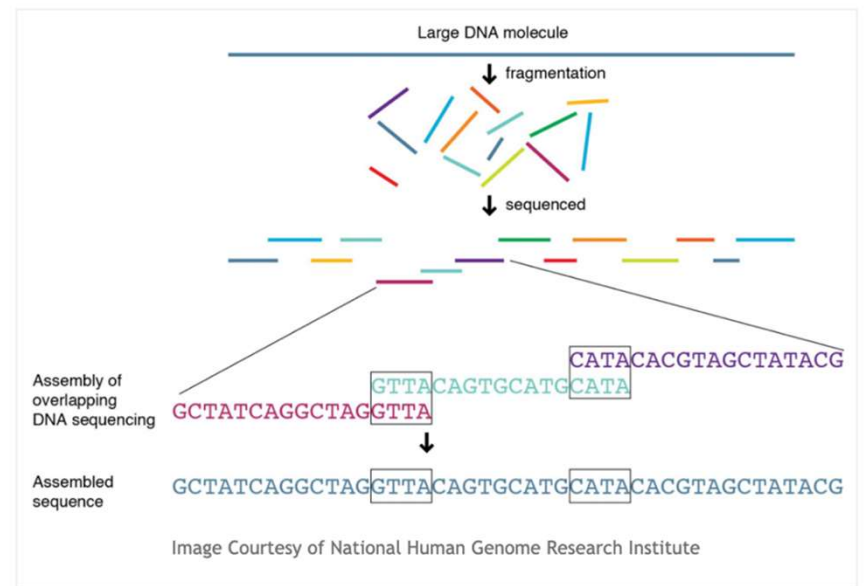
Identifies bacteria, viruses, fungi, and protists

Most accurate testing available

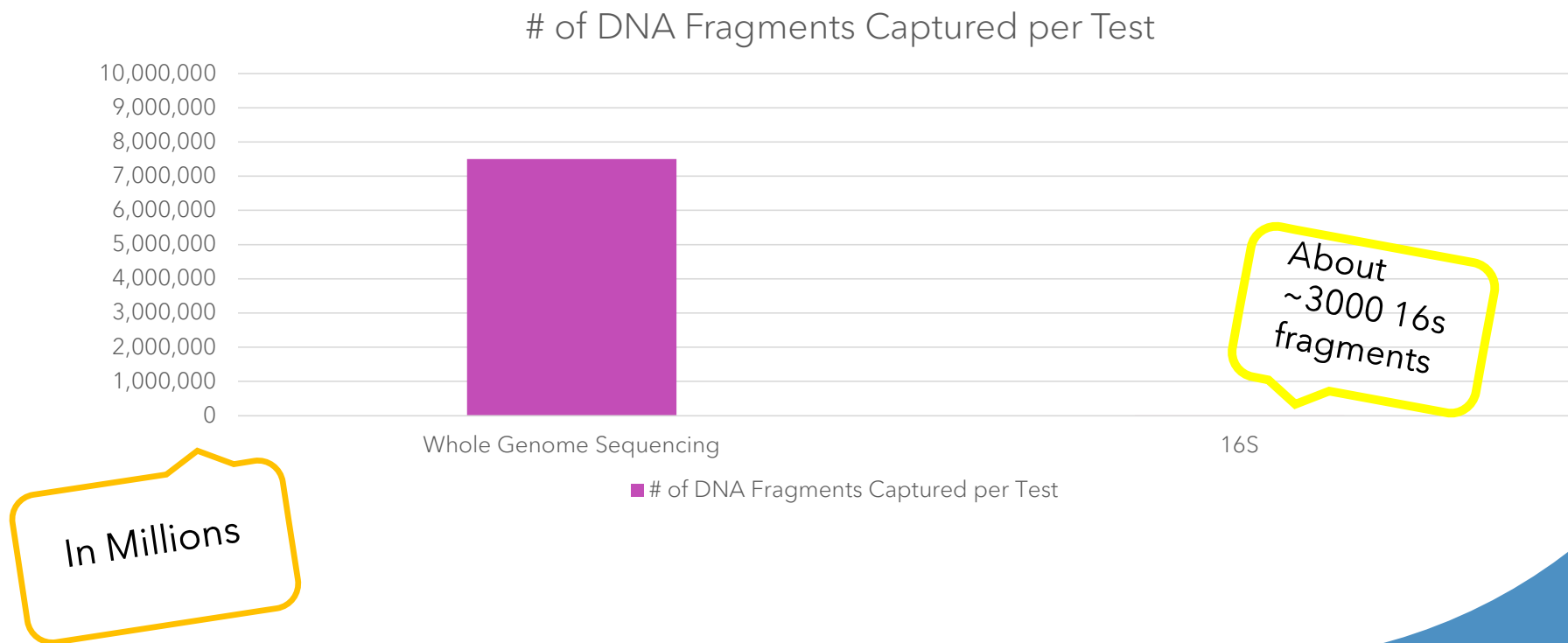
99.9% specificity

95.7% sensitivity

Like high definition (HD) resolution



DNA Capture Between Technologies




BiomeFX in IBS-C

Function Microbiome Analysis

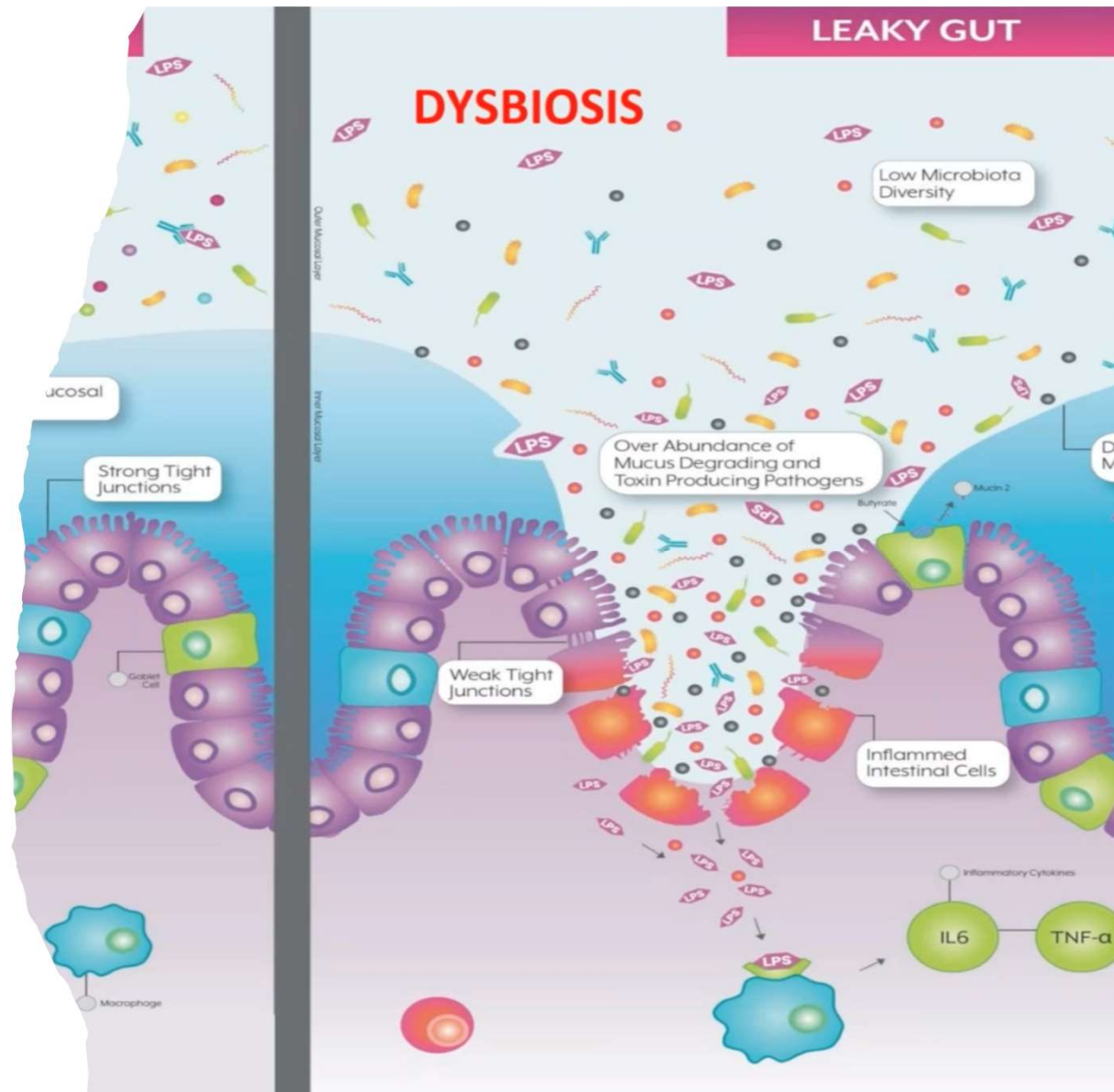


Case Study: Microbiome Pattern

- Following low fiber/low FODMAP diet
 - Afraid to eat many foods
 - Avoids gluten, dairy, corn
 - Bloating, constipation, excessive gas
 - Rosacea and acne, especially during menstrual cycle
 - Low alpha diversity, post Rifaxamin administration
 - High euryarchaeota
 - Low keystone species and SCFA production
 - High ammonia, histamine, and estrogen recycling
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Defining Dysbiosis

- Low alpha diversity
- An overgrowth of potentially harmful organisms
- Low keystone and commensal organisms



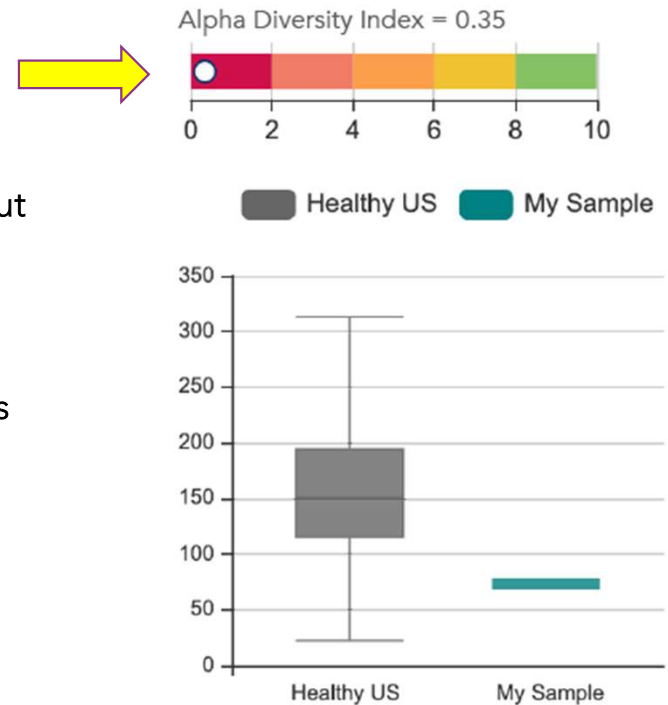
Quantity and Quality of Bacteria

- Alpha Diversity - Quantity

How many species in patient's gut compared to healthy US gut

- Beta Diversity - Quality

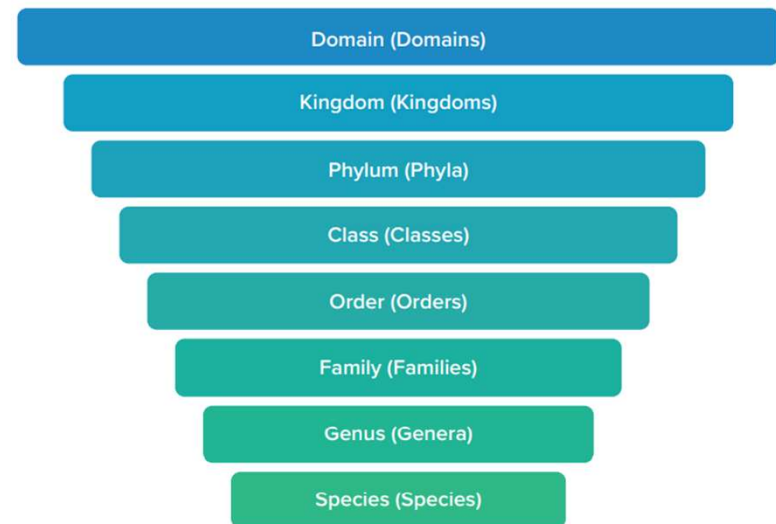
How the species identified in the gut compares to the species in the healthy US gut



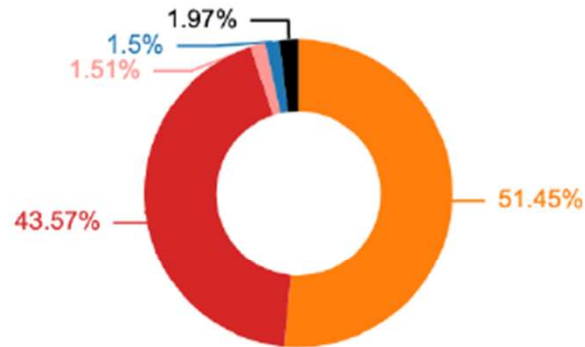
Phylum Level Microorganisms

- Gives us insights into overall pattern and balances
- In many ways it's more important than species level detection
- Sets the overall pattern for the rest of the test patterns

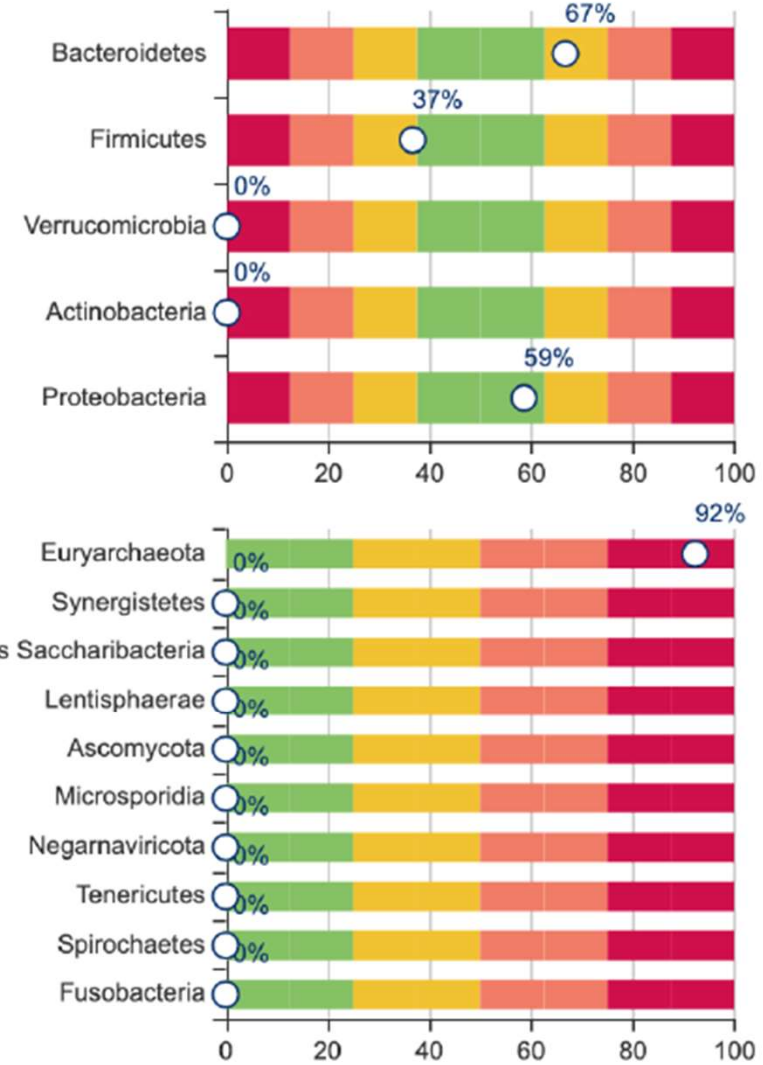
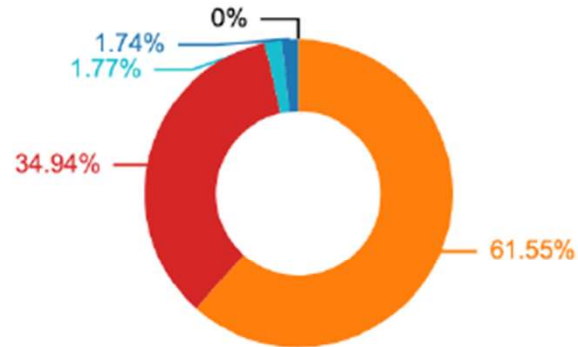
How Microbes Are Classified



Phylum Level US Healthy

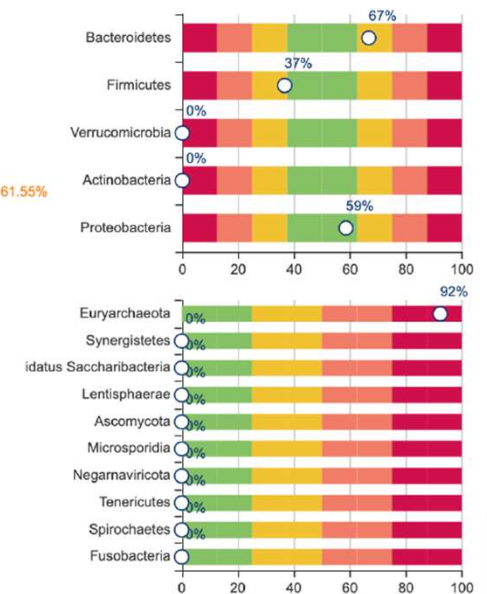
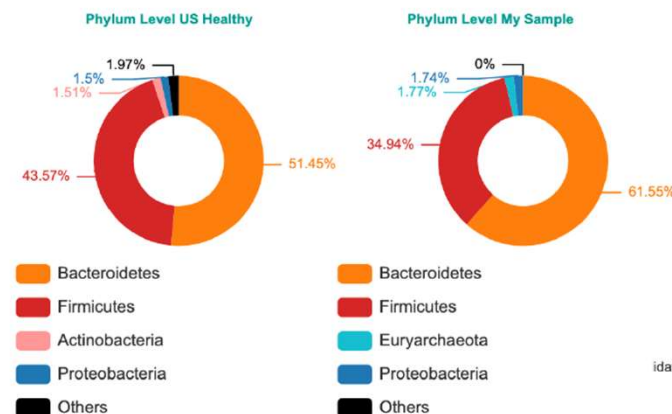


Phylum Level My Sample

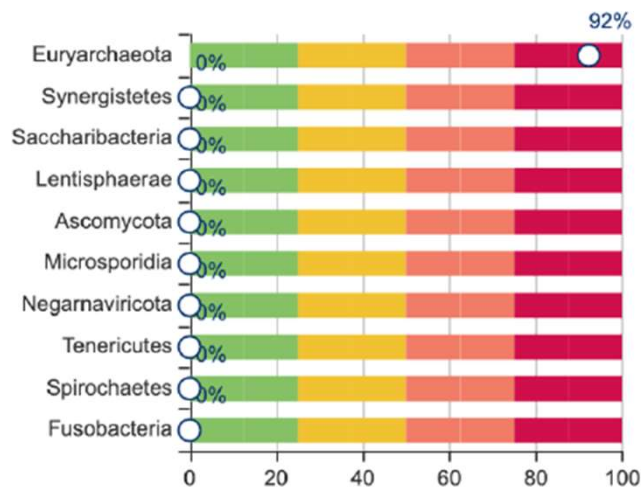


Phylum Level Composition

- **Bacteroidetes** should take up the biggest percentage
- **Firmicutes** contains the most keystone species but there are plenty of opportunistic groups residing in this phyla also.
- **Verrucomicrobia** is where Akkermansia muciniphilia lives
- **Actinobacteria** is where Bifido species reside
- **Proteobacteria** is the most inflammatory (LPS!). Aim for <2.739% overall relative abundance.
- **Euryarchaeota** is where methane producers reside



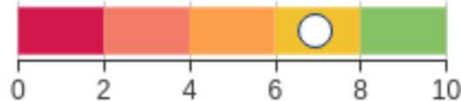
Phylum Level Gut Composition



- Euryarchaeota are methane producers (think constipation).
- Synergistetes often correlates with oral dysbiosis, gingivitis, and poor stomach acid.
- Ascomycota is the phylum for yeasts, fungi, and mold.
- Spirochaetes are where Borrelia (Lyme!) and Syphilis live
- Fusobacteria is very inflammatory and often associated with IBD, colorectal cancer.

Pathogenic & Pathobiont Organisms

Pathogen Control Index = 6.94



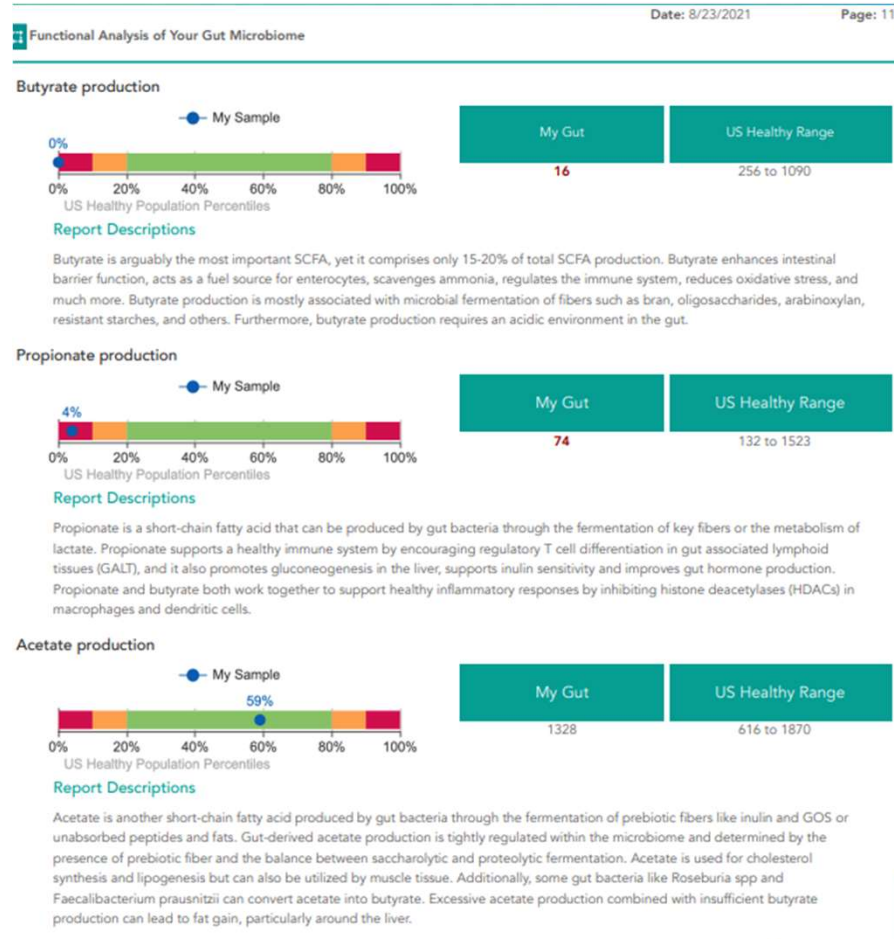
BiomeFX is NOT a diagnostic test. If your Pathogen levels are abnormally high consult your physician who can make a diagnosis and provide treatment if needed.

Pathogen Species	Healthy RA IQR %	My Sample RA %
Escherichia coli	0.04 - 0.47	0.2633
Klebsiella pneumoniae	0.02 - 0.22	0.2623
→ Bilophila wadsworthia	0.05 - 0.18	0.1894
Bacteroides fragilis	0.07 - 0.79	0.5644

Phylum	Family	Healthy Population Relative Abundance IQR Range [%]	My Sample Relative Abundance[%]	My Sample Percentile
Firmicutes	Streptococcaceae	0.04 - 0.37	0.92	90.44
Euryarchaeota	Methanobacteriaceae	0.05 - 0.68	1.99	93.02

SCFA Production

- Methanogens can feed off of acetate, shunting it's conversion to butyrate
- Measures the genes in the sample that code for SCFA production
- Low or absent levels of SCFA leads providers to make therapeutic recommendations



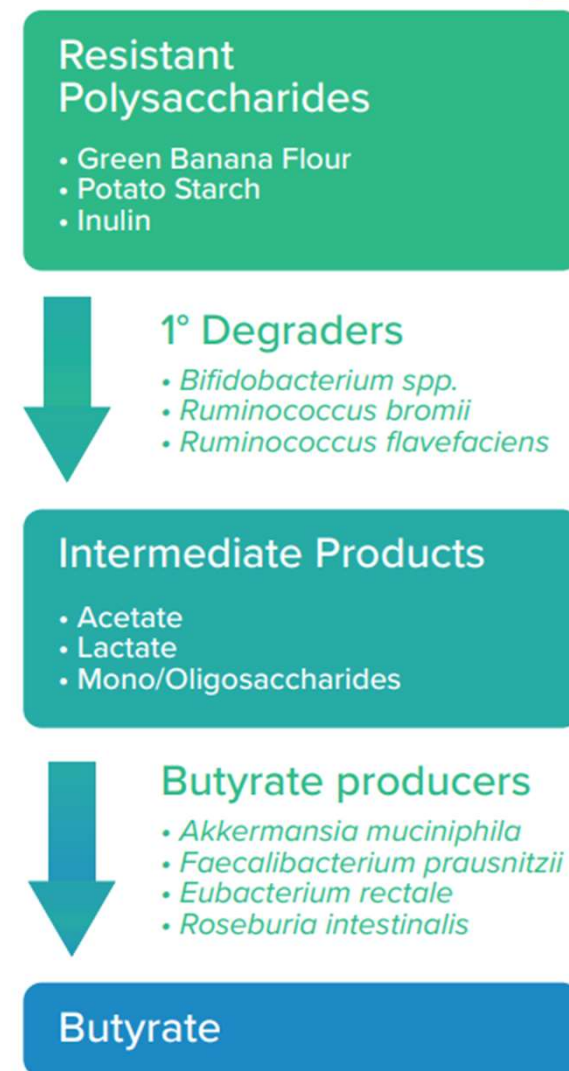
Depletion of Keystone Species

- Take up 1-3% of overall microbiome
- Most potent SCFA producers
- Keep intestinal pH slightly more acidic
- Play biggest role in gut-brain functioning
- Assist in microbiome-immune system cross talk

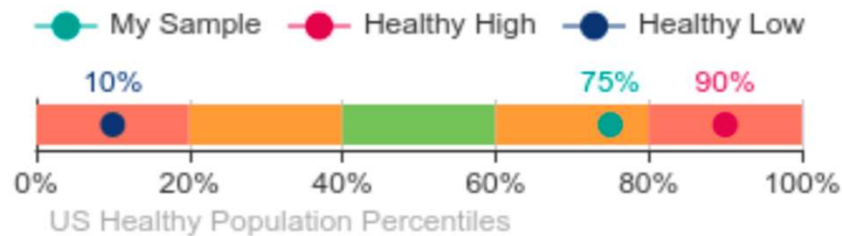
Keystone Species	Function	Healthy Relative Abundance IQR Range[%]	My Sample Relative Abundance
Phylum: Verrucomicrobia			
Akkermansia muciniphila	Acetate Producer	0.15 - 2.295	Not Detected
Phylum: Actinobacteria			
Bifidobacterium longum	Acetate Producer	0.127 - 1.268	Not Detected
Bifidobacterium adolescentis	GABA Producer	0.077 - 1.536	Not Detected
Phylum: Firmicutes			
Faecalibacterium prausnitzii	Butyrate Producer	0.675 - 2.032	0.562
Ruminococcus bromii	Cellulose Degradar	0.155 - 1.391	10.845
Ruminococcus flavefaciens	Cellulose Degradar	0.007 - 0.014	Not Detected
Roseburia intestinalis	Butyrate Producer	0.062 - 1.116	Not Detected
Eubacterium rectale	Butyrate Producer	0.665 - 2.238	Not Detected
Butyricicoccus pullicaecorum	Butyrate Producer	0.011 - 0.04	Not Detected
Lactobacillus rhamnosus	Lactate Producer	0.016 - 0.051	Not Detected
Lactobacillus reuteri	Lactate Producer	0.011 - 0.016	Not Detected
Total Lactobacillus species	Lactate Producer	0.032 - 0.196	Not Detected

Low FODMP or Not?

- Fermentable fibers feed our keystone species of bacteria
- They also feed methanogens
- Clinical use of a low-FODMAP diet should have parameters and an end-point
- You cannot starve your keystone species and expect to have a healthy gut microbiome



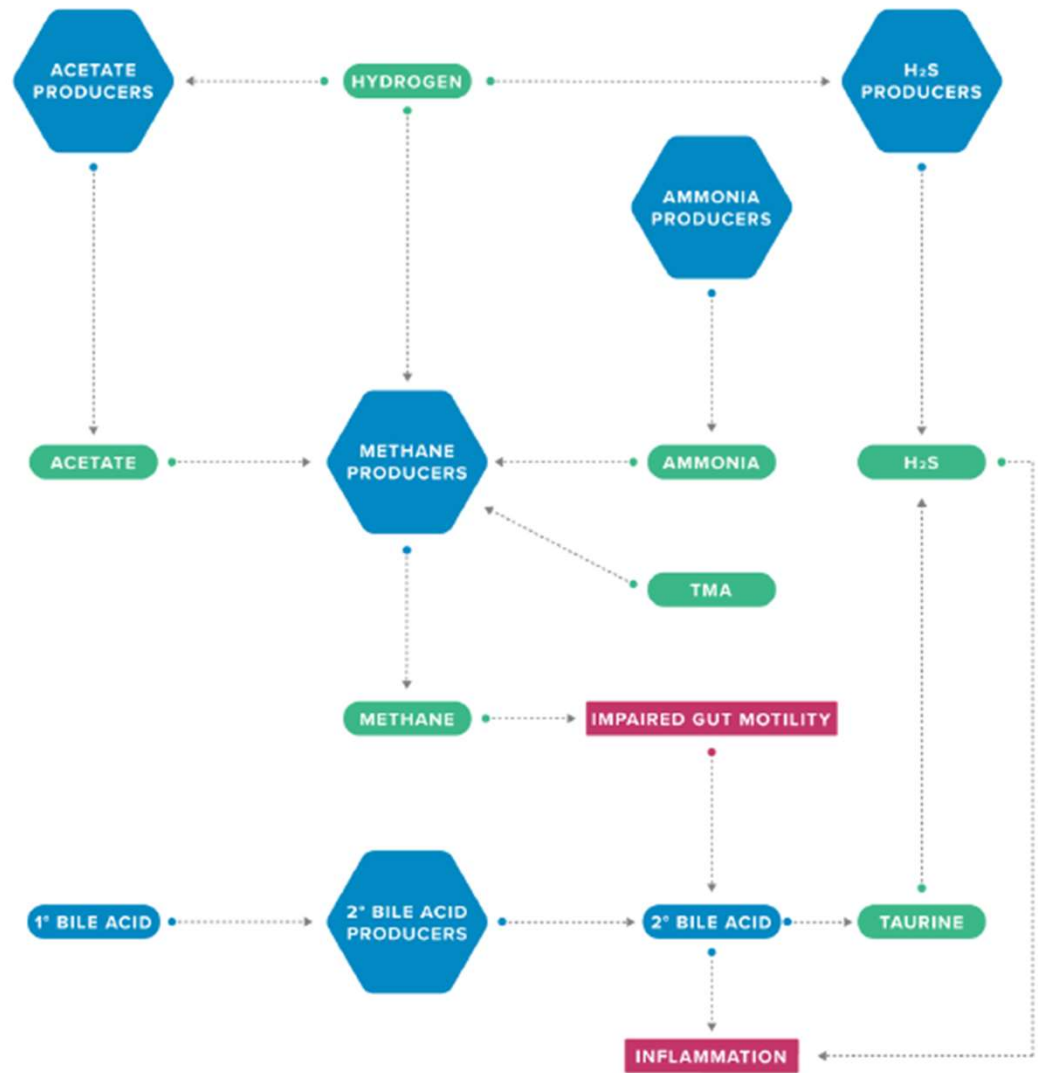
Methane production



- Remember the Euryarchaeota phylum was elevated. That is the first hint
- Archaea are not bacteria
- Methanogens can consume acetate, TMA, ammonia, and hydrogen to stay alive
- They consume acetate that should feed butyrate producers
- Prefer a more neutral intestinal pH to thrive
- Can lead to further intestinal inflammation

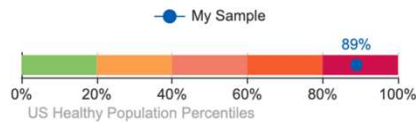
Methanogens

- Can feed off many substrates
 - Hydrogen
 - Acetate
 - Ammonia
 - TMA
- Methane cannot be utilized by human cells
 - Bloating, gas, slowed transit, weight gain
- Block the conversion of acetate to butyrate (gut-brain!)
- If you're not pooping, you're not detoxifying



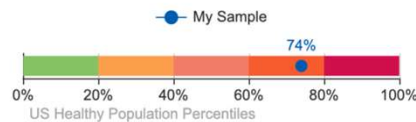
Other Notable Test Markers:

Ammonia production



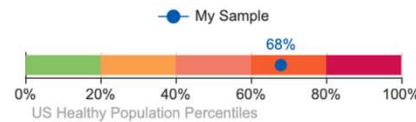
My Gut	US Healthy Range
0.2481	0.01 to 0.26

Histamine production



My Gut	US Healthy Range
0.1232	0 to 0.32

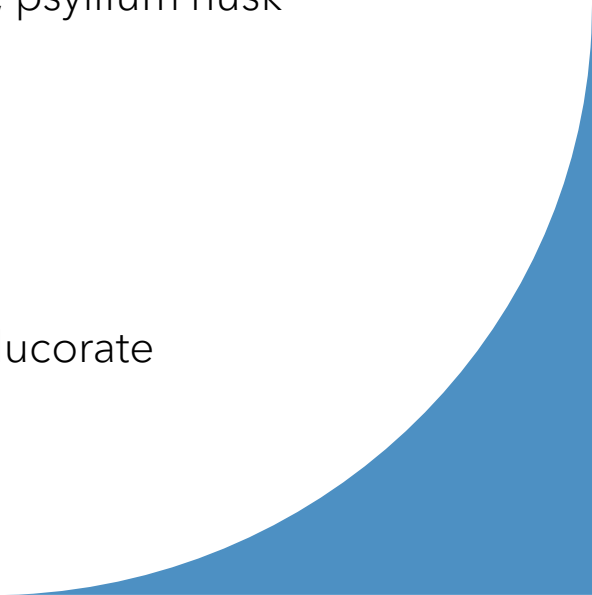
Estrogen recycling (Estrobolome)



My Gut	US Healthy Range
0.1301	0.06 to 0.24

- Ammonia can put strain on detox pathways and liver health
 - Secreted by many inflammatory groups
 - Glutamine feeds ammonia production
- Histamine production needs to be balanced with histamine breakdown
 - Can lead to mast cell degranulation and higher histamine levels internally
- High estrobolome needs to be corroborated with a hormone test. If elevated, recondition the gut to help lower b-glucuronidase secreting bacteria

Case Report Protocol:

- Rule out SIBO and test antibodies to vinculin
 - Methanogens/motility: ginger, licorice flavonoids, magnesium citrate, intermittent fasting, garlic/allicin.
 - Pathogens: *Saccharomyces boulardii* and HU58™
 - SCFAs: If no SIBO, rec'd oligosaccharides, resistant starch, sunfiber, psyllium husk
 - Keystone: Polyphenols, fibers, meditation, organics
 - Ammonia: support liver health
 - Histamine: consider a DAO supplement and quercetin
 - Estrobolome: test hormones but consider DIM and/or calcium d-glucorate
 - K2 trending low: 300mcg K2 QD
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Thank You

