



# The Wonderful Microbiome

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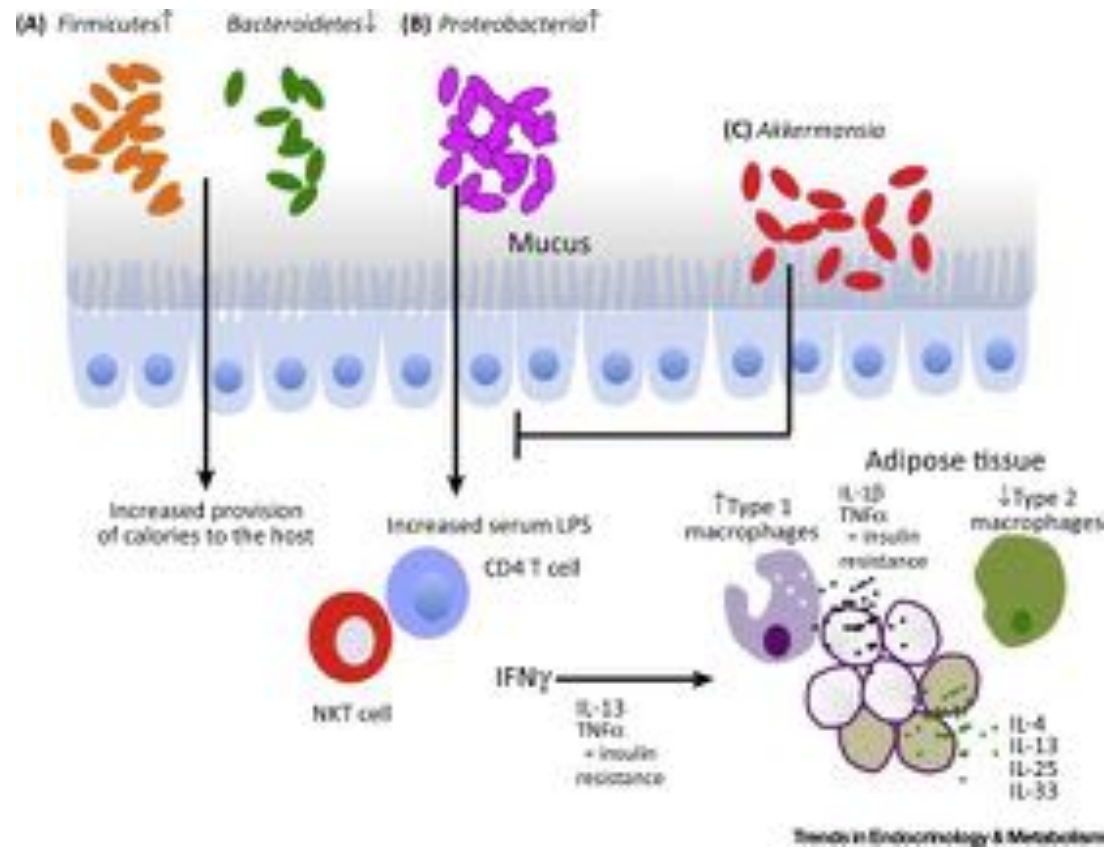
Just what is the  
microbiome?

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

-Joshua Lederberg

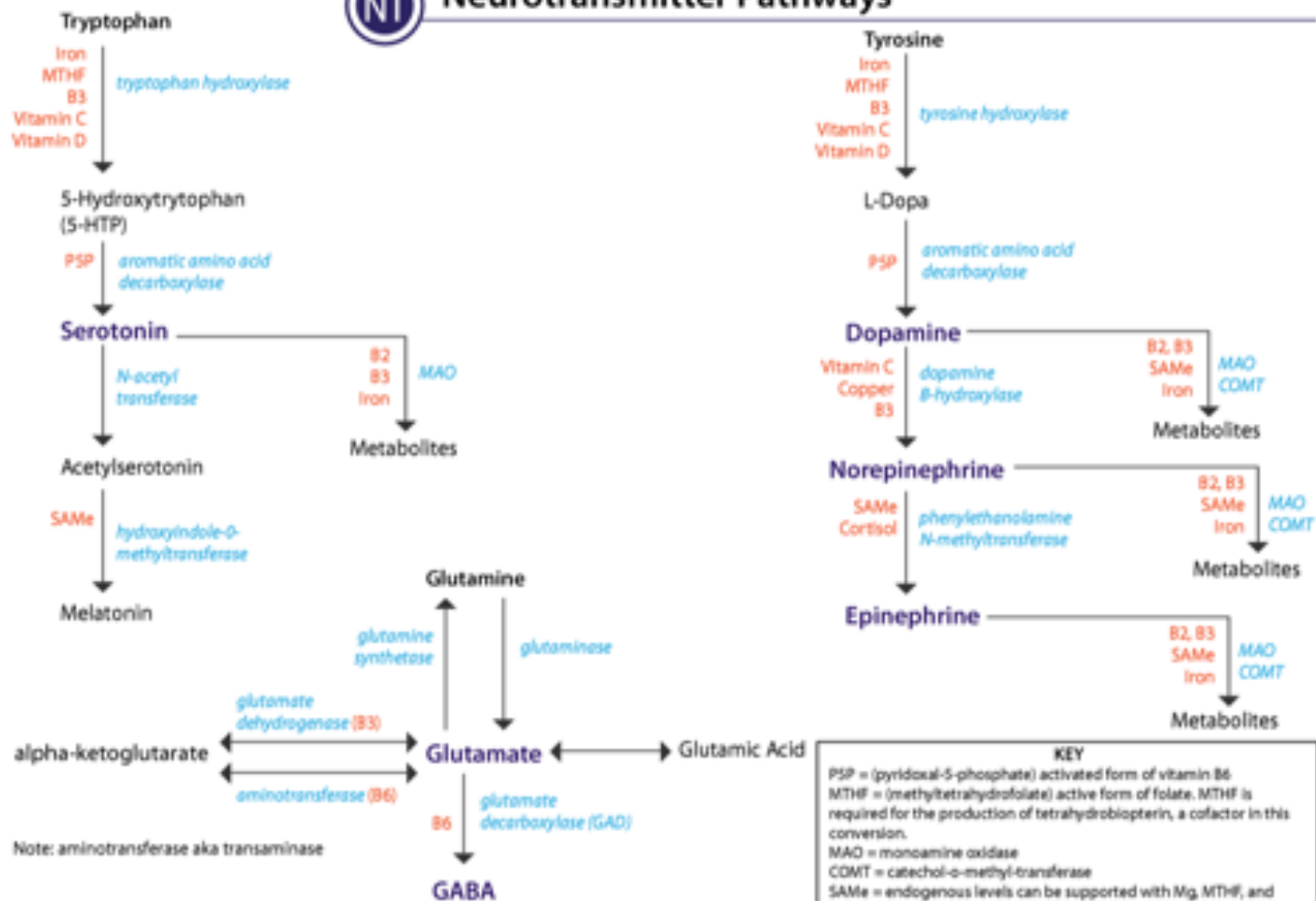
# Integrated with nearly all chronic diseases



- Mood
- Chronic inflammatory conditions
- Neuroinflammatory conditions
- Cancer
- Autism
- Metabolic problems – obesity, diabetes
- Liver diseases
- Skin disorders



# Neurotransmitter Pathways



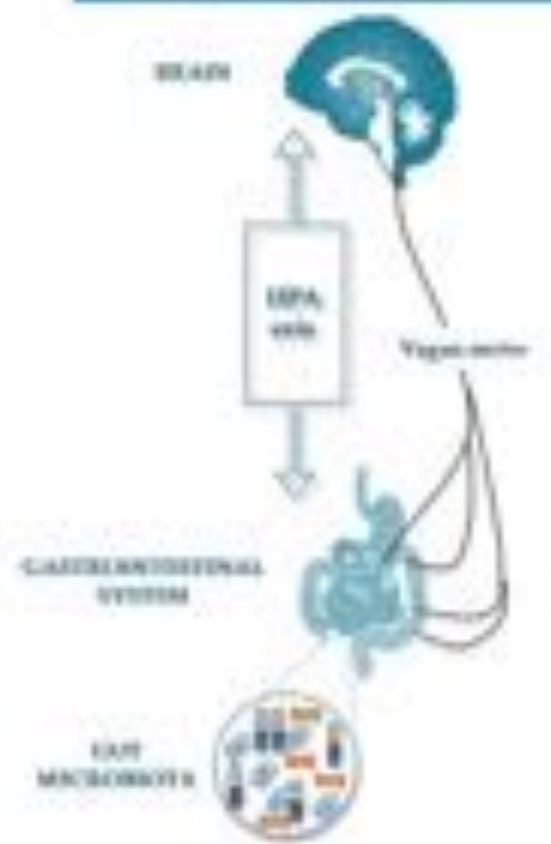
Note: aminotransferase aka transaminase

**KEY**

- PSP = (pyridoxal-5-phosphate) activated form of vitamin B6
- MTHF = (methyltetrahydrofolate) active form of folate. MTHF is required for the production of tetrahydrobiopterin, a cofactor in this conversion.
- MAO = monoamine oxidase
- COMT = catechol-O-methyl-transferase
- SAMe = endogenous levels can be supported with Mg, MTHF, and methylcobalamin supplementation
- Cofactors = ■ Enzymes = ■

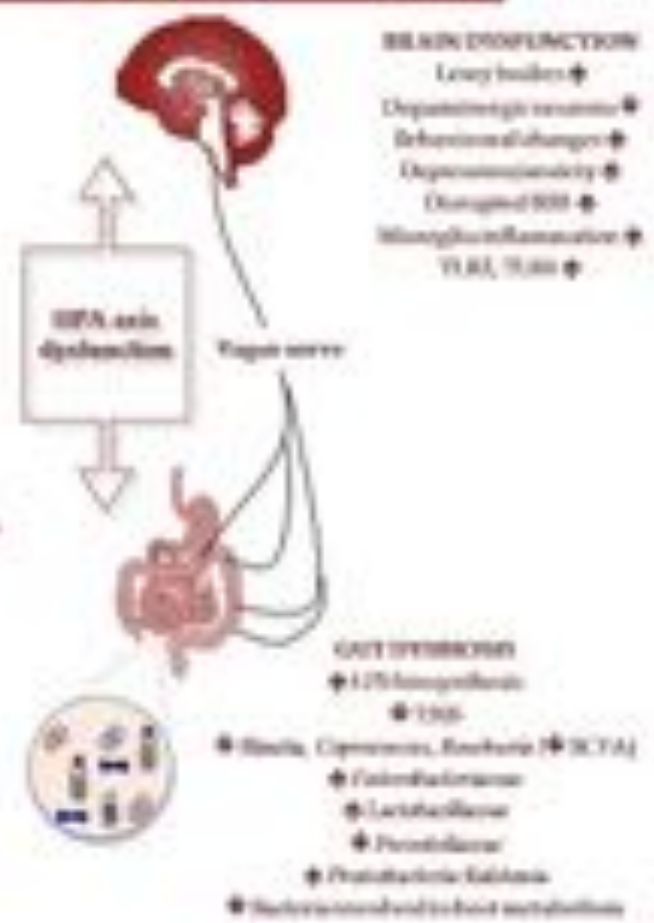


**Healthy microbiota get from a job**



BBB - Blood Brain Barrier  
 HP - *Helicobacter pylori*  
 LPS - Lipopolysaccharides  
 PD - Parkinson's disease

**Microbiota get brain axis and TLRs in PD**

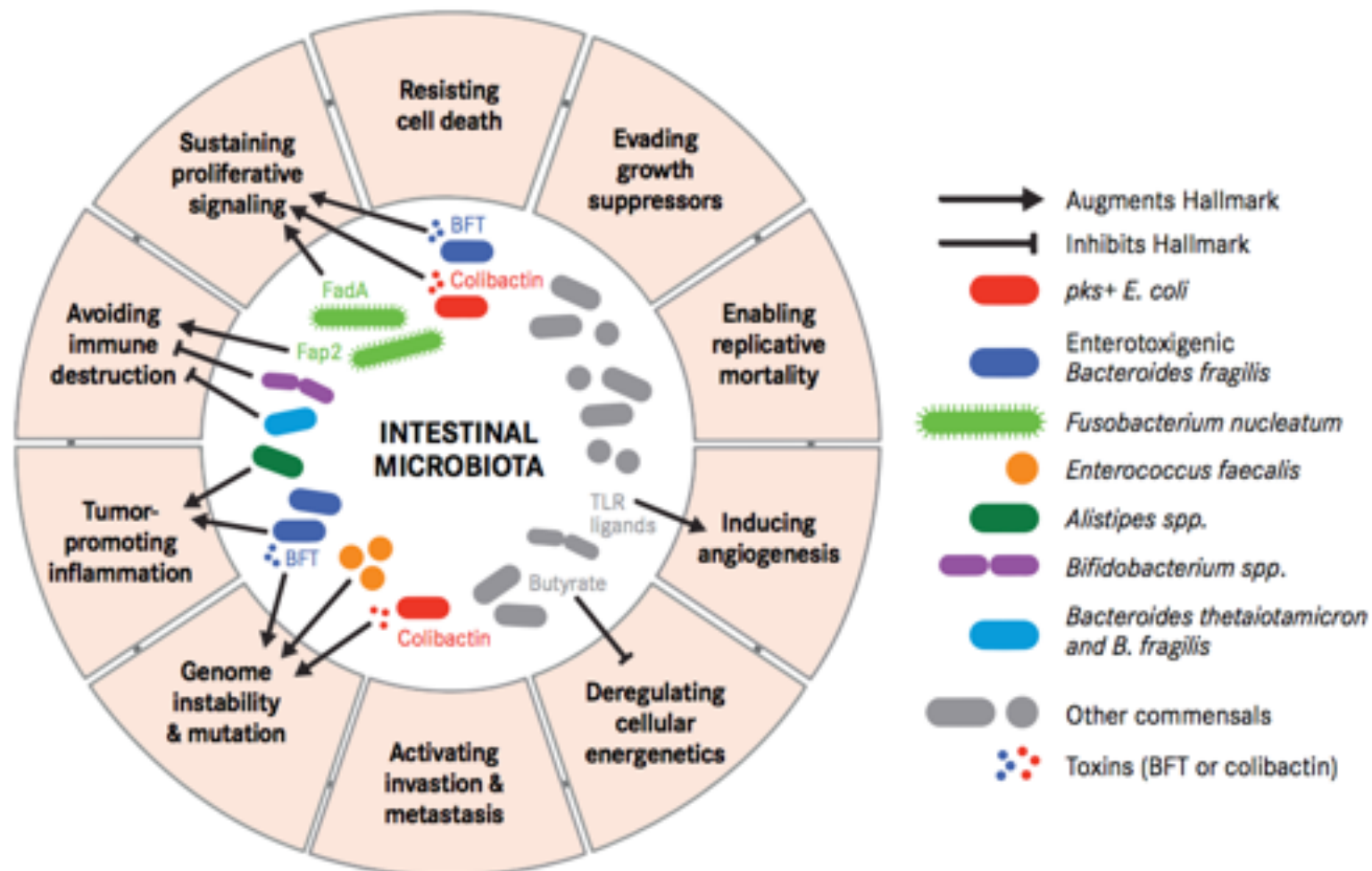


**BRAIN DYSFUNCTION**  
 ↓  
 Lewy bodies  
 ↓  
 Dopaminergic neurons  
 ↓  
 Behavioral changes  
 ↓  
 Depressiveness  
 ↓  
 Damaged BBB  
 ↓  
 Microglial Inflammation  
 ↓  
 TLR2, TLR4

**GUT DYSFUNCTION**  
 ↓  
 Lewy bodies  
 ↓  
 Dopaminergic neurons  
 ↓  
 Abdominal pain  
 ↓  
 Constipation  
 ↓  
 Nausea  
 ↓  
 Gut inflammation  
 ↓  
 Gut permeability  
 ↓  
 Peptidases  
 ↓  
 HP activation  
 ↓  
 TLR2, TLR4

**GUT DYSBIOSIS**  
 ↓  
 ↓ LPS biosynthesis  
 ↓ TSS  
 ↓ Bifida, Coprococcus, Eubacterium (SCFA)  
 ↓ Clostridiaceae  
 ↓ Lactobacillus  
 ↓ Prevotellaceae  
 ↓ Proteobacteria: Sphingobacteria  
 ↓ Streptococcus and other variations

SCFA - short chain fatty acids  
 TSS - type II secretion system  
 TLR2 - Toll like receptor 2  
 TLR4 - Toll like receptor 4



BFT indicates *Bacteroides fragilis* toxin; *pks+*, colibactin-producing; TLR, toll-like receptor.

A growing body of clinical evidence has uncovered links between the microbiota and the Hallmarks of Cancer. These include butyrate, a short-chain fatty acid; colibactin, a genotoxin; and FadA and Fap2, bacterial mechanisms of *Fusobacterium nucleatum*.

Fulbright LE, Ellermann M, Arthur JC. The microbiome and the hallmarks of cancer. *PLoS Pathog.* 2017;13(9):e1006480. doi:10.1371/journal.ppat.1006480.

# The Future - there is a lot we don't know

- Genomic testing only recently available
- The Microbiome Project
- Claire Fraser-Liggett and Dr. Shuldiner – energy and obesity
- NIH – 162 clinical trials recruiting in the United States

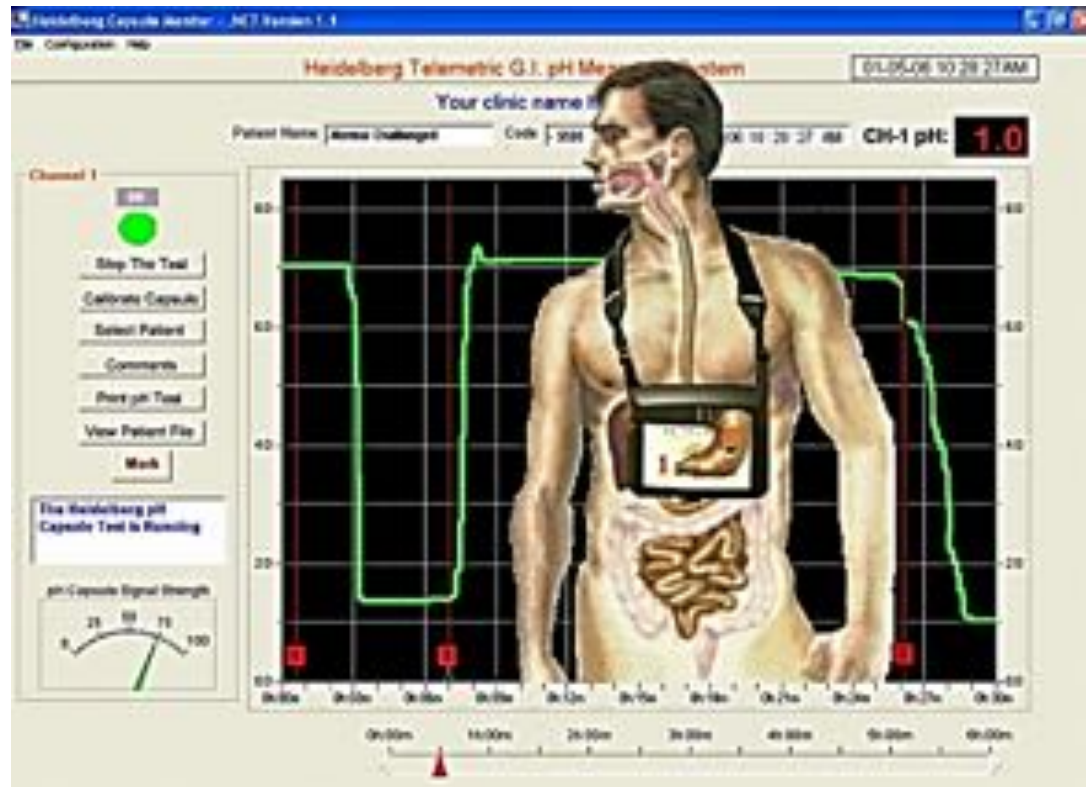


# Not just the gut

- Dr. Blaser – organisms of the skin and psoriasis
- Jacques Ravel and Larry J. Forney – 200 women and bacterial vaginosis
- Dr. Storch – viruses in the blood that cause serious pediatric fevers – 20 million hospital visits a year
- Lung, skin, and brain pathogens

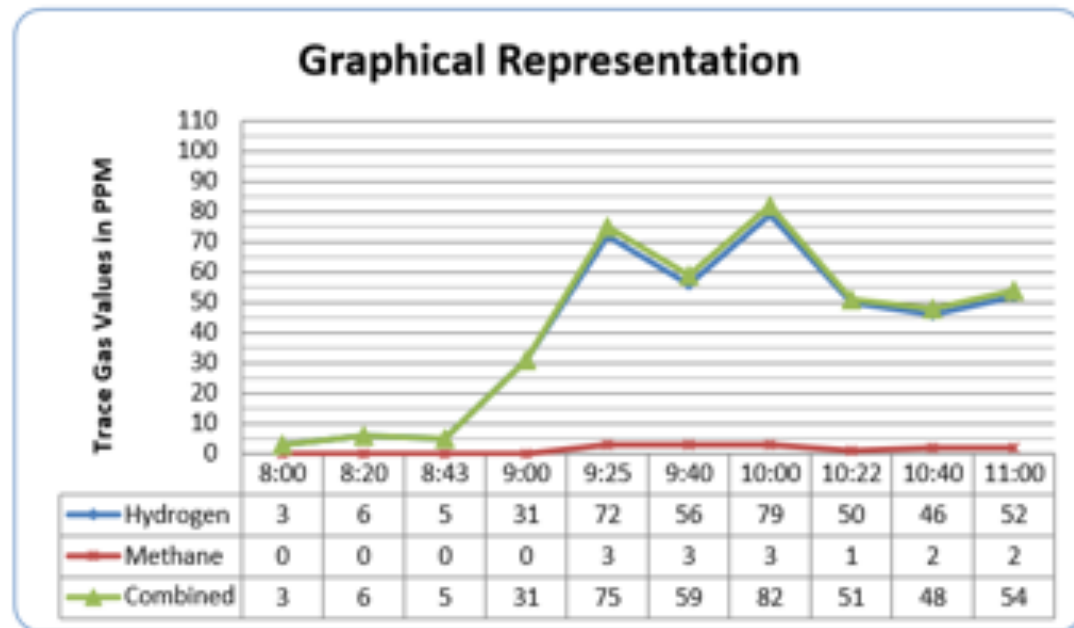


# Diagnostics - stomach



- Heidelberg test – stomach acid
- Betaine Hcl supplementation

# Diagnostics – small intestine



- Small Intestinal Bacteria Overgrowth (SIBO)
- Food allergy and sensitivity testing (IgE and IgG) - "leaky gut"
- Amino acid blood test
- Neurotransmitter urine test

RESULT		- REFERENCE RANGE -			ALLERGEN	- NOT SAFE -		
		LOW	MODERATE	AVOID		LOW	MODERATE	AVOID
213	Avoid	<70	70 - 100	>100	CANDIDA SCREEN			
					Candida albicans			
					DAIRY			
376	Avoid	<100	100 - 350	>350	Casein			
268	Avoid	<100	100 - 250	>250	Cheddar Cheese			
636	Avoid	<100	100 - 350	>350	Cottage Cheese			
824	Avoid	<140	140 - 350	>350	Cow's Milk			
192	Moderate	<120	120 - 370	>370	Goat's Milk			
289	Moderate	<100	100 - 350	>350	Mozzarella Cheese			
338	Moderate	<150	150 - 400	>400	Parmesan			
361	Avoid	<100	100 - 350	>350	Sheep Milk			
1357	Avoid	<150	150 - 250	>250	Whey			
344	Moderate	<150	150 - 400	>400	Yogurt			
					FISH			
124	Low	<200	200 - 350	>350	Cod			
70	Low	<190	190 - 340	>340	Halibut			
87	Low	<200	200 - 350	>350	Salmon			
70	Low	<150	150 - 300	>300	Sardine			
87	Low	<160	160 - 310	>310	Sole			
89	Low	<250	250 - 400	>400	Tilapia			
85	Low	<200	200 - 350	>350	Trout			
70	Low	<150	150 - 300	>300	Tuna			
					FRUITS			
101	Low	<160	160 - 310	>310	Apple Mix			
72	Low	<120	120 - 270	>270	Apricot			
459	Avoid	<150	150 - 300	>300	Avocado			
82	Low	<160	160 - 340	>340	Banana			
101	Low	<160	160 - 310	>310	Blackberry			
99	Low	<130	130 - 280	>280	Blueberry			
89	Low	<160	160 - 310	>310	Boysenberry			
106	Low	<150	150 - 300	>300	Cantaloupe			
143	Low	<180	180 - 330	>330	Cherry			
69	Low	<100	100 - 250	>250	Cranberry			
100	Low	<150	150 - 300	>300	Currants			
149	Low	<180	180 - 330	>330	Fig			
96	Low	<150	150 - 300	>300	Grapefruit			
237	Moderate	<150	150 - 300	>300	Kiwi			
75	Low	<130	130 - 280	>280	Lemon			
69	Low	<100	100 - 250	>250	Mango			
115	Low	<130	130 - 280	>280	Orange			
174	Low	<180	180 - 310	>310	Papaya			
73	Low	<120	120 - 270	>270	Peach			

Analyte	Result	Unit per Creatinine	L	WRI	H	Reference Interval
Phenethylamine (PEA)	27	nmol/g				28 - 70
Tyrosine	112	μmol/g				28 - 75
Tyramine	1.9	μmol/g				1.6 - 3.2
<b>Dopamine</b>	211	μg/g				110 - 200
3,4-Dihydroxyphenylacetic acid (DOPAC)	331	μg/g				330 - 1000
3-Methoxytyramine (3-MT)	175	nmol/g				82 - 174
<b>Norepinephrine</b>	21	μg/g				18 - 42
Normetanephrine	133	μg/g				70 - 275
<b>Epinephrine</b>	4.3	μg/g				1.3 - 7.3
Metanephrine	55	μg/g				44 - 103
Norepinephrine / Epinephrine ratio	4.9					< 12
Tryptamine	0.3	μmol/g				0.10 - 0.75
<b>Serotonin</b>	83	μg/g				50 - 98
5-Hydroxyindolacetic acid (5-HIAA)	1450	μg/g				1600 - 6000
<b>Glutamate</b>	42	nmol/g				9.0 - 40.0
<b>Gamma-aminobutyrate (GABA)</b>	2.8	nmol/g				1.6 - 3.5
Glycine	2805	nmol/g				350 - 1500
Histamine	32	μg/g				12 - 30
Taurine	1111	μmol/g				240 - 900
Creatinine	125	mg/dL				35 - 240

# Diagnostics – large intestine

BACTERIOLOGY CULTURE	
<b>Commensal (Imbalanced) flora</b>	<b>Dysbiotic flora</b>
4+ Alpha hemolytic strep	4+ Citrobacter koseri
2+ Hemolytic Escherichia coli	4+ Enterobacter cloacae complex
1+ Proteus mirabilis	4+ Klebsiella oxytoca
	4+ Klebsiella pneumoniae ssp pneumoniae
	2+ Possible Salmonella spp Sent to State for Confirmation

- Comprehensive stool analysis + parasitology x3: also tells us about pancreatic function
- Fecal occult immunoassay
- Inflammatory Bowel Disease blood screen
- Celiac disease blood screen
- C-reactive protein

# Diagnostics - other

- Viruses such as EBV, CMV, HSV-6, Hepatitis panel
- Urinalysis
- Immune marker blood testing – CBC, cytokines, Th1/Th2
- Hashimoto's – thyroid antibody screening
- Lyme disease
- STI testing

## Comprehensive Stool Analysis / Parasitology x1

DIGESTION / ABSORPTION				
	Within	Outside	Reference Range	
Elastase	410		> 200 $\mu\text{g/mL}$	Elastase findings can be used for the diagnosis or the exclusion of exocrine pancreatic insufficiency. Correlations between low levels and chronic pancreatitis and cancer have been reported. <b>Fat Stain:</b> Microscopic determination of fecal fat using Sudan IV staining is a qualitative procedure utilized to assess fat absorption and to detect steatorrhea. <b>Muscle fibers</b> in the stool are an indicator of incomplete digestion. Bloating, flatulence, feelings of "fullness" may be associated with increase in muscle fibers. <b>Vegetable fibers</b> in the stool may be indicative of inadequate chewing, or eating "on the run". <b>Carbohydrates:</b> The presence of reducing substances in stool specimens can indicate carbohydrate malabsorption.
Fat Stain	None		None - Mod	
Muscle fibers	Rare		None - Rare	
Vegetable fibers	Rare		None - Few	
Carbohydrates	Neg		Neg	

INFLAMMATION				
	Within	Outside	Reference Range	
Lactoferrin		8.0	< 7.3 $\mu\text{g/mL}$	Lactoferrin and Calprotectin are reliable markers for differentiating organic inflammation (IBD) from functional symptoms (IBS) and for management of IBD. Monitoring levels of fecal lactoferrin and calprotectin can play an essential role in determining the effectiveness of therapy, are good predictors of IBD remission, and can indicate a low risk of relapse. <b>Lysozyme*</b> is an enzyme secreted at the site of inflammation in the GI tract and elevated levels have been identified in IBD patients. <b>White Blood Cells (WBC)</b> and <b>Mucus</b> in the stool can occur with bacterial and parasitic infections, with mucosal irritation, and inflammatory bowel diseases such as Crohn's disease or ulcerative colitis.
Calprotectin*		85	$\leq 50 \mu\text{g/g}$	
Lysozyme*	78		$\leq 600 \text{ ng/mL}$	
White Blood Cells	None		None - Rare	
Mucus	Neg		Neg	

# Treatment Options

- Antibacterial and antifungals
  - Rifaximin, berberine, colloidal silver, oil of oregano, caprylic acid, undecylic acid, bacteriophages, probiotics
- Fecal transplant – FDA?!?
  - The Power of Poop (taken down)?
  - The Fecal Transplant Foundation
- Helminths
  - [helminthictherapywiki.org](http://helminthictherapywiki.org)
- Transit time helpers
  - Ginger, fiber, 5-HTP, Jujube, bitters, hydration, vitamin C, magnesium