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2025 EDITION

INTERPRETIVE GUIDE

GI-MAP® – Unparalleled DNA-Based Stool Testing

Our mission: to deliver innovative, accurate and clinically relevant diagnostic testing in a timely and cost-effective manner

GI-MAP®

GI Microbial Assay Plus

GI-MAP®

GI Microbial Assay Plus

FIRST OF ALL

THANK YOU

FOR CONSIDERING US!

"At Diagnostic Solutions Laboratory, we're not content with the range of clinical testing currently available to practitioners. We believe that every patient should achieve optimal health, and we're driven to give clinicians the tools to do so. Our mission, therefore, is to use our resources to bring the most advanced, innovative, and clinically relevant testing to healthcare providers worldwide."

Tony Hoffman
President and CEO

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GI-MAP®

INTRODUCTION

The Gastrointestinal Microbial Assay Plus (GI-MAP®) is an innovative clinical tool that measures gastrointestinal microbiota DNA from a single stool sample with state of the art, quantitative polymerase chain reaction *(qPCR or real-time PCR)* technology.

The GI-MAP was designed to detect microbes that may be disturbing normal microbial balance or contributing to illness as well as indicators of digestion, absorption, inflammation, and immune function. The following guide may be useful for understanding the nature of each of the microorganisms found on the GI-MAP, as well as clinical implications and treatment guidelines.

Please see the GI-MAP white paper for additional, fully referenced, information.

HOW TO READ THE REPORT

GI-MAP quantifies bacteria, fungi, viruses, and parasites using qPCR. This is a leap forward from older methodologies that report only positive or negative. Results are reported as colony forming units per gram of stool (CFU/g). One CFU is roughly equivalent to one microorganism *(or one cell)*. Results are expressed in standard scientific notation. A reported result of 3.5e7 is equivalent to 3.5 x 10^7 CFU/g, which equals 35,000,000 CFU/g, or 35 million CFU per gram of stool.

PATHOGENS

BACTERIAL PATHOGENS	Result		Reference
Campylobacter	< dl		< 1.00 e3
C. difficile Toxin A	1.21 e5	High ↑	< 1.00 e3

Figure 1. The normal reference range for *C. difficile,* Toxin A is 0–1,000 CFU/g. The patient's result is very high at 1.21 x 10^5, or 121,000 CFU/g.

Reference ranges were developed using known positive, diseased samples to construct cut off values that distinguish disease-causing amounts of pathogenic and opportunistic microbes. Reference ranges for the pathogens were correlated with an FDA cleared assay for GI pathogens. The GI-MAP is capable of detecting as low as 0.1 cell per gram of stool.

Table 1. Scientific notation; a basic reference table.

1.0e1	1 X 10^1	10	Ten
1.0e2	1 X 10^2	100	One hundred
1.0e3	1 X 10^3	1,000	One thousand
1.0e4	1 X 10^4	10,000	Ten thousand
1.0e5	1 X 10^5	100,000	One hundred thousand
1.0e6	1 X 10^6	1,000,000	One million

PATHOGENS

The GI-MAP includes pathogens *(bacterial, parasitic, and viral)* commonly known to cause intestinal gastroenteritis. It's important to note that not all individuals with positive findings for pathogens will present with symptoms. Many factors, including the health of the individual, the transient nature of some pathogens, and the presence and expression of virulence factors all contribute to an individual's symptoms. Toxins are a type of virulence factor produced by certain pathogens. Since GI-MAP is a DNA-based test, results reflect the levels of pathogenic strains carrying the toxin genes, not the levels of any toxins that may be produced.

BACTERIAL PATHOGENS

Campylobacter

- **Epidemiology**
  - » One of the most common causes of foodborne illness in the U.S.
  - » Fecal contamination of poultry and water
- **Clinical Implications**
  - » May be infectious at very low exposures
  - » Symptoms range from mild to severe abdominal pain, diarrhea, fever, malaise; lasting several days to several weeks
  - » Vast majority of those with symptoms of gastroenteritis recover without treatment
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin level to determine GI inflammation
  - » Consider high dose probiotics, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*
  - » Heavy infections can be treated with azithromycin and fluoroquinolones

Table 2. Clinical Approach — *The Five "R" Treatment Protocol.*

The 5R Protocol is a widely accepted clinical guideline to treating pathogens and imbalances in the GI microbiota and restoring health to the gastrointestinal tract. Re-test patients with the GI-MAP in 3–6 months to monitor progress and make changes to the treatment protocol as needed.

REMOVE Using a course of antimicrobial, antiviral, antifungal, or antiparasitic therapies in cases where these organisms are present. It may also be necessary to remove offending foods, gluten, or medication that may be acting as antagonists.	**Antimicrobial**	Broad-spectrum antimicrobial herbs including: berberine, caprylic acid, garlic oil, oil of oregano, uva ursi, olive leaf extract
	Antibiotics	Research the recommended antibiotic for the specific microbe present. Avoid medications to which the microbe is thought to have resistance.
	Antifungal	Caprylic acid, garlic oil, oil of oregano, olive leaf extract
	Antiparasitic	Black walnut, garlic oil, oil of oregano, Artemisia (wormwood), berberine, goldenseal, gentian root extract, quassia bark extract, citrus seed extract
	Antiviral	Olive leaf extract, purified silver, cat's claw, monolaurin, osha root (*Ligusticum porteri*), vitamin A, vitamin C, vitamin D, reishi mushrooms, *Echinacea*, zinc
REPLACE In cases of maldigestion or malabsorption, it may be necessary to restore proper digestion by supplementing with digestive enzymes.	**Digestive support**	Betaine hydrochloride, apple cider vinegar, herbal bitters, ox bile, lactase, pancreatic enzymes (amylase, lipase, protease), pepsin
REINOCULATE Recolonization with healthy, beneficial bacteria. Supplementation with probiotics, along with the use of prebiotics helps re-establish the proper microbial balance.	**Probiotics**	*Lactobacillus acidophilus, Bifidobacterium bifidum, Bifidobacterium longum, Lactobacillus rhamnosus, Bifidobacterium breve, Lactobacillus casei, Saccharomyces boulardii*
	Prebiotics	Beta-glucan, fiber, inulin, pectin, xylooligosaccharides, galactooligosaccharides, larch arabinogalactans
REPAIR Restore the integrity of the gut mucosa by giving support to healthy mucosal cells, as well as immune support.	**Immune Support**	Colostrum, immunoglobulins, *S. boulardii*
	Intestinal Barrier Repair	L-Glutamine, aloe vera extract, deglycyrrhizinated licorice, marshmallow root, okra, N-acetyl glucosamine, quercetin, *S. boulardii,* slippery elm, zinc carnosine, vitamin A, essential fatty acids, B vitamins
REBALANCE Address whole body health and lifestyle factors so as to prevent future GI dysfunction.	**Support Consideration**	Sleep, diet, exercise, and stress management

Clostridium difficile, Toxin A and Toxin B

The GI-MAP tests only for the genes for toxin A and toxin B, which are carried by *C. difficile*. The GI-MAP does not measure toxins directly for any microbe.

- **Epidemiology**
  - » 2–10% of population are carriers, most are asymptomatic
  - » Prolonged use of antibiotics may be causative factor
- **Clinical Implications**
  - » Symptoms include inflammation, abdominal pain, cramping, fever, and diarrhea
  - » Symptoms often present during antibiotic use and often subside once antibiotics are discontinued
  - » Gastrointestinal (GI) infection can cause reactive arthritis
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and secretory IgA (SIgA) levels to determine GI inflammation and immune response
  - » Consider *Saccharomyces boulardii,* high dose probiotics, broad-spectrum antimicrobial herbs, and 5R Protocol *(see Table 2)*
  - » Mild infections can be treated with metronidazole
  - » Heavy infections can be treated with vancomycin and fidaxomicin
  - » Asymptomatic patients may not need treatment
  - » In asymptomatic patients with positive toxins A and/or B, the genes are likely not *"turned on,"* and thus not causing disease. It is still prudent to avoid antibiotics in these patients to prevent CDAD. Consider antimicrobial herbal formulas, which can suppress *C. diff* without activating toxin production.
  - » Additional testing for toxins A and B may be warranted

E. coli

Escherichia coli is a gram-negative, facultative anaerobic bacterium of the genus *Escherichia.* The organism is commonly found in the lower intestine of warm-blooded organisms. There are many different pathotypes, or subtypes, of *E. coli* and the organism can share genes rapidly within and between pathotypes. GI-MAP measures 6 different gene types of *E. coli. (See Table 3)*

- **Epidemiology**
  - » Fecal contamination of food *(undercooked beef, raw milk, and unpasteurized juice)* and water
  - » Fresh and under washed produce (ex. lettuce, spinach, sprouts) are common sources of *E. coli* contamination
- **Clinical Implications**
  - » Symptoms of classic pathogenic *E. coli* infection are watery and/or bloody diarrhea. This presentation is much more likely with the Shiga-like Toxin genes present.
  - » Other symptoms can include fever, fatigue, abdominal cramping, nausea, and diarrhea
  - » There may be no symptoms, especially with low levels of genes detected

- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin, eosinophil activation protein (EAP) and SIgA levels to determine GI inflammation and immune response
  - » Management of *E. coli* infection is usually hydration and rest, and the infections are often transient and self-resolving depending on immune system competence
  - » Asymptomatic patients may not need treatment
  - » Antibiotics may be contraindicated; they can initiate HUS
  - » Consider high-dose probiotics (300+ billion CFU/day)
  - » Consider bacteriophages, broad-spectrum antimicrobial herbs, and/or 5R Protocol *(see Table 2)*

⚠ HEMOLYTIC UREMIC SYNDROME (HUS)

Hemolytic uremic syndrome is one of the more serious potential outcomes of an *E. coli* infection. This is kidney damage induced by the Shiga-like Toxin, produced by some pathotypes of *E. coli*. It can lead to some serious end results such as hemolytic anemia, thrombocytopenia, kidney damage, and even death.

The risk factors for hemolytic uremic syndrome include: age (more common in children than in adults); severe prolonged infections; and the use of antibiotics.

Importantly, Enterohemorrhagic *E. coli* (EHEC) and Shiga-like Toxin *E. coli*-STEC are classic for resulting in hemolytic uremic syndrome.

Antibiotic use is typically contraindicated when there is the presence of a Shiga-like Toxin detected. Many healthcare practitioners adopt standard practice to not use antibiotics at all when *E. coli* is detected.

E. coli Pathotypes

The subtypes of *E. coli* are referred to as pathotypes. This is an area of research that is constantly evolving and nomenclature of pathotypes evolves accordingly.

The table below can help you identify which *E. coli* pathotypes relate to the *E. coli* gene targets measured on GI-MAP.

Table 3. Interpretation of different *E. coli* pathotypes based on gene targets identified on GI-MAP.

GI-MAP® MARKER	*E. coli* PATHOTYPES / STRAIN					
	EPEC	EIEC	ETEC	EHEC	STEC	*E. coli* O157:H7
E. coli EPEC/EHEC (eae)	■			■		■
E. coli O157						■
Enteroinvasive *E. coli*/Shigella		■				
Enterotoxigenic *E. coli* LT/ST			■			
Shiga-like Toxin *E. coli* stx1				■	■	■
Shiga-like Toxin *E. coli* stx2				■	■	■

One or both of the Shiga-like Toxin genes can be present for EHEC, O157:H7, or STEC

■ *E. coli* Gene
■ Toxin Gene

Table 4. Description *E. coli* markers found on GI-MAP

GI-MAP MARKER	DESCRIPTION
***E. coli* - EPEC/EHEC**	A single gene that can be found on the genome of either enteropathogenic or enterohemorrhagic *E. coli*. Interpret with other *E. coli* genes detected on GI-MAP to distinguish between the two.
E. coli O157	May be found on some pathogenic strains of *E. coli,* but this finding by itself is not a pathogenic marker. If seen by itself this is an outer membrane protein.
Enteroinvasive *E. coli/Shigella*	A gene that can be found on either EIEC or *Shigella*.
Enterotoxigenic *E. coli LT/ST*	Either the LT or ST gene-the heat-labile and heat stable genes. This is a toxin gene and would be found on ETEC or enterotoxigenic *E. coli.* This is the most common cause of traveler's diarrhea, and 95% of cases are self-limiting.
Shiga-like Toxic *E. coli* stx1	Shiga-like Toxin gene. Caution with antibiotic use for hemolytic uremic syndrome (HUS).
Shiga-like Toxic *E. coli* stx2	Shiga-like Toxin gene. Caution with antibiotic use for HUS.

SOURCES OF EXPOSURE AND RE-INFECTION

To effectively treat infections and prevent reinfection, exposure should be identified and eliminated. Most exposure to pathogens occurs via fecal-oral transmission, most often due to use of contaminated water sources or improper hand hygiene. This may include drinking contaminated water, eating raw foods washed in contaminated water or harvested *(e.g. shellfish)* in contaminated water, or improper handwashing.

To remove microorganisms from food, the FDA recommends first washing your hands, running cool water over fruits and vegetables, while rubbing or scrubbing, and then letting them dry out before eating. During treatment, consider all possible sources of fecal transmission: romantic partners, children *(especially if in diapers or not toilet-trained)*, sheets, towels, water source to the home, etc...

Salmonella

- **Epidemiology**
  - » Fecal contamination of ingested foods *(eggs, poultry, meat, unpasteurized milk, raw fruits, and vegetables)*
  - » Exposure to pets *(reptiles, amphibians, baby chicks)*
- **Clinical Implications**
  - » May be asymptomatic
  - » Symptoms include fever, vomiting, and severe diarrhea
  - » Typically self limiting within seven days
  - » GI infection can cause reactive arthritis and may be involved in ankylosing spondylitis
  - » Systemic infections may require treatment with antibiotics
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » Remove sources of infection
  - » Consider high-dose probiotics (300+ billion CFU/d)
  - » Consider broad-spectrum antimicrobial herbs and 5R Protocol *(see Table 2)* Antibiotics are contraindicated; they may cause relapse of infection

Table 5.

FOOD SOURCES OF SALMONELLA
Poultry and poulty products
Meat and diary
Raw, fresh, ready-to-eat produce such as: berries, tomatoes, leafy greens, sprouts, and melons

Vibrio cholerae

- **Epidemiology**
  - » Fecal contamination of ingested foods *(raw shellfish)* and often picked up during international travel
- **Clinical Implications**
  - » May be asymptomatic or cause mild symptoms
  - » Severe infections present with profuse watery diarrhea *("rice-water stools"),* vomiting, rapid heart rate, loss of skin elasticity, thirst, dry mucous membranes, low blood pressure, restlessness, or irritability
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response.
  - » Rehydration therapy
  - » Zinc, especially in children
  - » Consider probiotics, broad-spectrum antimicrobial herbs and 5R Protocol *(see Table 2)*
  - » Heavy infections may be treated with doxycycline

Yersinia enterocolitica

- **Epidemiology**
  - » Fecal contamination of ingested foods and liquids *(water, undercooked pork, meats, and dairy products)*
- **Clinical Implications**
  - » Symptoms usually develop four to seven days after exposure and are self-limiting
  - » Symptoms include water or bloody diarrhea, fever, vomiting, and abdominal pain *(may resemble appendicitis)*
  - » Symptoms may mimic Crohn's disease
  - » May trigger autoimmune thyroiditis or inflammatory arthritis in susceptible individuals
- **Therapeutic Approaches & Considerations**
  - » Consider probiotics, broad-spectrum antimicrobial herbs and 5R Protocol *(see Table 2)*
  - » Heavy infections can be treated with doxycycline in combination with an aminoglycoside
  - » Trimethoprim-sulfamethoxasole, chloramphenicol, and rifaximin may also be useful treatments

PARASITIC PATHOGENS

Cryptosporidium

Epidemiology
- » Fecal contamination of ingested foods and liquids *(contaminated water and swimming pools, undercooked meat, and raw milk)*
- » Common cause of traveler's diarrhea

- **Clinical Implications**
  - » Symptoms typically last 2–3 weeks and are self-limiting
  - » If symptoms persist, look for sources of contamination, such as drinking water
  - » Can cause reactive arthritis
- **Therapeutic Approaches & Considerations**
  - » May not require treatment
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » If necessary, consider anti-parasitic herbal treatments containing ingredients such as black walnut, garlic oil, oil of oregano, Artemisia (wormwood), berberine, goldenseal, gentian root extract, quassia bark extract, citrus seed extract
  - » Consider probiotics and 5R Protocol *(see Table 2)*
  - » Search for and remove sources of fecal contamination
  - » Heavy infections can be treated with nitazoxanide*

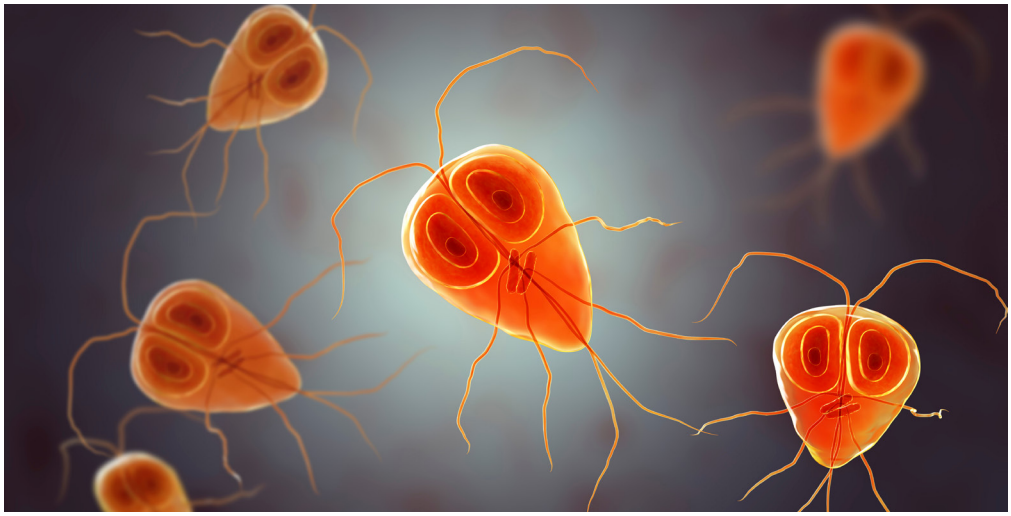
Entamoeba histolytica

- **Epidemiology**
  - » Fecal contamination of ingested foods or water
  - » Pets may be a source of exposure
  - » Sexual contact may be a source of exposure
- **Clinical Implications**
  - » Symptoms include diarrhea, fulminating colitis *(resembling ulcerative colitis),* and dysentery
  - » Extreme cases may invade liver and lung tissues
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » Treatment may be indicated, even in asymptomatic carriers
  - » Mild infections can be treated with Iodoquinol, paromomycin, or diloxanide furoate*
  - » Moderate to heavy infections can be treated with metronidazole or tinidazole, followed by iodoquinol or paromomycin*
  - » If appropriate, consider anti-parasitic herbal treatments *(see Table 2)*
  - » Consider probiotics and 5R Protocol *(see Table 2)*
  - » Avoid reinfection by fecal contamination

Giardia

- **Epidemiology**
  - » Most commonly isolated protozoan worldwide
  - » Found in outside water sources *(lakes, streams, ponds)* and can get past filtration systems
  - » Carried by animals
  - » Common in daycare workers
- **Clinical Conditions**
  - » May be asymptomatic, especially in patients with adequate levels of normal bacteria and SIgA
  - » Symptoms include acute diarrhea, bloating, cramps, weight loss, intestinal malabsorption, and steatorrhea
  - » Can cause urticaria or neurologic symptoms such as irritability, sleep disorder, or depression
  - » May cause malnutrition and vitamin B12 deficiency
  - » Can cause reactive arthritis
- **Therapeutic Approaches & Considerations**
  - » See patient's calprotectin and SIgA levels to determine GI inflammation and immune response
  - » Infections can be treated with tinidazole, nitazoxanide, metronidazole, paramomycin, furazolidone, or quinacrine*
  - » Consider probiotics and 5R Protocol *(see Table 2)* to repair and rebuild the gut mucosa

** Additional information (dosing, efficacy, etc.) on pharmaceutical treatment for parasites may be found at www.cdc.gov/parasites/index.html and in the Physician's Desk Reference.*



Giardia intestinalis protozoan

VIRAL PATHOGENS

Adenovirus 40/41

- **Epidemiology**
  - » Common cause of diarrhea in infants and children but can also affect adults
  - » Mainly transmitted by fecal contamination *(fecal-oral route)*
- **Clinical Implications**
  - » Causative agents of gastrointestinal disease and gastroenteritis
  - » Symptoms include fever and watery diarrhea, usually limited to 1–2 weeks
  - » May also be present in the stool of asymptomatic carriers and may not require treatment
- **Treatment**
  - » Handwashing
  - » Hydration
  - » Antiviral herbs such as cat's claw, osha root, reishi mushrooms, vitamins A, C, and D, zinc, Echinacea
  - » Address other imbalances on the GI-MAP and use 5R Protocol *(see Table 2)* to rebuild gut health and gut immunity

Norovirus GI/GII

- **Epidemiology**
  - » Fecal contamination of ingested foods and water
  - » Common cause of stomach flu on cruise ships
  - » Common cause of non-bacterial gastroenteritis and outbreaks in the world
- **Clinical Implications**
  - » Symptoms include nausea and vomiting, diarrhea, abdominal cramps, low-grade fever, muscle aches, fatigue, and headache
  - » Generally short-lived, lasting about 24–72 hours
- **Treatment**
  - » Antivirals are not recommended
  - » Supportive care for the gastric mucosa, hydration, and immune-boosting agents may be warranted
    - – Handwashing
    - – Hydration
    - – Antiviral herbs such as cat's claw, osha root, reishi mushrooms, vitamins A, C, and D, zinc, Echinacea
    - – Address other imbalances on the GI-MAP and use 5R Protocol *(see Table 2)* to rebuild gut health

H. pylori AND VIRULENCE FACTORS

Helicobacter pylori (H. pylori)

Recent studies have shown that nearly 50% of the world's population may harbor *H. pylori*. And, although many carriers are asymptomatic, *H. pylori* is known to have a causative role in ulcers, chronic gastritis, and stomach cancer. Additionally, in early phases of colonization, patients may experience hypochlorhydria followed by a change to hyper aciduria. Over time, additional *H. pylori* strains may colonize, including those with Virulence Factors and increased disease potential.

- **Epidemiology**
  - » Fecal contamination, oral to oral, and family inter-infection are common modes of transmission
- **Clinical Implications**
  - » Dyspepsia, abdominal pain, nausea, vomiting and chronic gastrointestinal symptoms
  - » Peptic ulcers
  - » May induce mucosal atrophy and metaplastic changes

Virulence Factors

Of the 50% of the population believed to be infected with *H. pylori*, only 2% develop gastric cancer. Positive *H. pylori* virulence factors on the GI-MAP represent the ***genetic potential*** for an *H. pylori* strain to cause pathology. For example, some clinicians may choose an aggressive treatment protocol for a patient with dyspepsia and a family history of gastrointestinal cancer, who shows elevated *H. pylori* and positive virulence factors. *(See Table 6)*

- **Treatment**
  - » Asymptomatic patients may not require treatment
  - » Consider herbal formulas to eradicate or suppress *H. pylori.* Ingredients may include: deglycyrrhizinated licorice, mastic gum, methylmethionine sulfonium chloride, vitamin C, zinc carnosine, bismuth citrate, berberine, goldenseal, oil of oregano, grape extract, Chinese goldthread extract, yerba mansa extract
  - » See pancreatic elastase-1 to determine if maldigestion and/or hypochlorhydria might be present
  - » Consider high-dose probiotics and 5R Protocol *(see Table 2)*

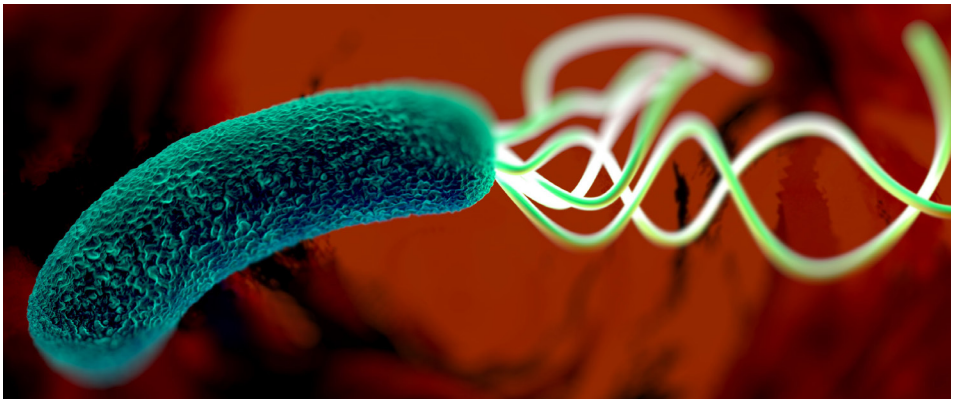
- Rebuild healthy gastric mucosa by reducing stress and giving soothing and healing agents such as glutamine, aloe, DGL, and vitamin A
- Address dental hygiene; the mouth is a reservoir for *H. pylori*
- Consider sources of exposure, especially romantic partners or family members
- Address other imbalances on the GI-MAP
- For peptic ulcer disease, the first-line triple therapy *(prescription)* treatment includes a proton pump inhibitor, clarithromycin, and amoxicillin or metronidazole
- Fluoroquinolones and tetracycline are used in second-line regimens against *H. pylori*
- See the GI-MAP Antibiotic Resistance Genes results for *Helicobacter* when designing an antibiotic protocol

H. PYLORI ANTIBIOTIC RESISTANCE GENES

	Result	Reference
Clarithromycin	**Positive**	Negative
Genes associated with clarithromycin resistance		
A2142C	Absent	
A2142G	Absent	
A2143G	**Present**	

Figure 2. An example antibiotic resistance gene measured on the GI-MAP for *H. pylori*. Number and letter combinations are single nucleotide polymorphisms (SNPs), or gene targets, that are involved in *H. pylori* drug resistance. If any SNP is detected *(present)*, then the *H. pylori* strain/s are resistant to that class of antibiotics. In this example, the patient's *H. pylori* is resistant to the clarithromycin class of antibiotics and it would be prudent to use a different antibiotic when tailoring a treatment protocol.

Note: In supporting individuals with H. pylori, consider the patient history, clinical symptoms, virulence genes, and the amount of H.pylori DNA detected in order to design a customized treatment plan.



Helicobacter pylori bacterium

Table 6. *H. pylori* virulence factors and disease associations.

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Helicobacter pylori Virulence Factors

Quick Reference Guide

The virulence factor genes on GI-MAP® are found exclusively on the genome of *H. pylori*.

These genes code for proteins that will predispose one to more serious *H. pylori* infections.
The chart below provides details of each virulence factors tested on the GI-MAP.

Gene Acronym	Gene Name	Genetic Characteristics	Associations with Disease
BabA	Blood Group Antigen Binding Adhesion	• Promotes DNA breakage in host cell • Improves *H. pylori* adherence ("stickiness") to epithelial cells • May promote other virulence factors, especially CagA	May promote carcinogenesis
CagA	Cytotoxin Associated Gene A	• Promotes *H. pylori* adhesion and colonization • Affects barrier function of gastric epithelial tight junctions • Promotes loss of cell polarity • Antagonizes VacA • Evades the immune system and affects the activity of dendritic cells and B-cells. • Considered part of the "pathogenicity island" which includes VirB and VirD virulence factors. This is a closely-associated group of genes that work synergistically and often transfer as a unit.	Promotes carcinogenesis, strong association. Also associated with peptic ulcer disease
DupA	Duodenal Ulcer-Promoting Gene A	• Promotes inflammation	Associated with duodenal ulcers, specifically
IceA	Induced by Contact with Epithelium A	• Transcription of this gene is only initiated after adhesion to the gastric epithelium • Promotes inflammation and associated with elevated IL-8	Associated with dyspepsia and gastric & duodenal ulcers NOT associated with gastric cancer
OipA	Outer Inflammatory Protein A	• Promotes inflammation • Drives IL-8 production	Associated with carcinogenesis and peptic ulcer disease
VacA	Vacuolating Toxin A	• Enters the host cell by endocytosis • Affects mitochondrial function • Disrupts tight junctions • Causes a programmed necrosis by inducing the production of large vacuoles inside the host cells; inducing cellular swelling; disrupting cell barrier thus causing nutrient leakage • Facilitates nutrient acquisition (iron, minerals, amino acids, etc.) • Inhibits antigen presentation in vitro • Antagonizes CagA	Associated with gastric inflammation, peptic ulcer disease, and gastric cancers
VirB & VirD		• Part of the CagA "pathogenicity island" • Both genes can potentiate CagA virulence factor by aiding in its transmission to host epithelial cels • In the absence of CagA, these virulence factors are unlikely to change clinical outcome of *H. pylori* infections.	Evaluate next to CagA virulence factors. VirB & VirD, if positive, can potentiate CagA virulence and clinical associations

- **How To Target Treatments in the Presence of Virulence Factors:**
  - » Generally, when virulence factors are present, the treatment goal will be to fully eradicate the *H. pylori* population. This can be confirmed by retesting the full GI-MAP, the pathogen panel, or the *H. pylori* panel 4–6 weeks after completing treatment. The goal is to achieve a result of <dl on the retest. The exception to this may be VirB and VirD if they are found in isolation (without CagA present).
  - » Below is a chart of treatment considerations for each of the virulence factors. These would be used in addition to the standard treatments for *H. pylori* alone.

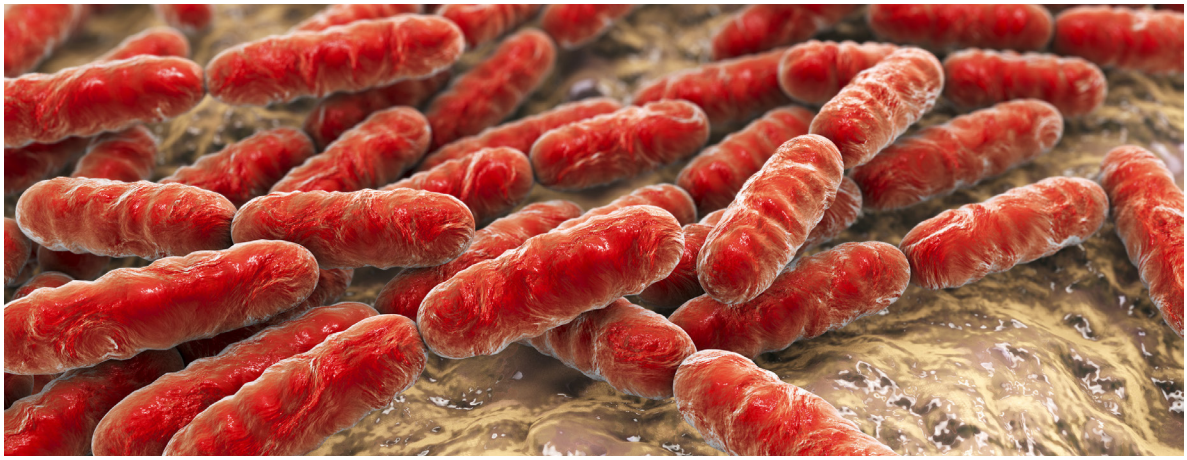
Table 6a. *H. pylori* virulence factors and treatment considerations.

Virulence Factor	Special Treatment Considerations
BabA	More aggressive treatment may be warranted; consider the use of adhesion inhibitions, particularly cranberry
CagA	Target inflammatory support, promote T-cell activity, consider curcumin, resveratrol/red wine, ginger, Nigella sativa, low salt diet
DupA	Consider the use of demulcents for mucosal protection
IceA	Inflammatory support, consider the use of adhesion inhibitors
OipA	Inflammatory support
VacA	Mitochondrial support, consider Nigella sativa, green tea, red wine/resveratrol, Scutellaria baicalensis
VirB & VirD	No additional treatments necessary

Please see the GI-MAP white paper for additional, fully referenced, information.

COMMENSAL/ KEYSTONE BACTERIA

Trillions of microorganisms inhabit the human intestine to make up a complex ecosystem that plays an important role in human health. Commensal bacteria extract nutrients and energy from our diets, maintain gut barrier function, produce vitamins *(biotin and vitamin K),* and protect against colonization by potential pathogens.



Bacteria Lactobacillus, lactic acid bacteria which are part of normal flora of human intestine

THE FOLLOWING COMMENSAL/KEYSTONE BACTERIA ARE REPORTED ON THE GI-MAP

Table 7.

COMMENSAL BACTERIA	
Bacteroides fragilis	Gram-negative species of the *Bacteroidetes* phylum. Immune-modulating normal gut species. Believed to be involved in microbial balance, barrier integrity, and neuroimmune health (Hsiao 2013). High levels may result from reduced digestive capacity or constipation. Low levels may contribute to reduced anti-inflammatory activity in the intestine.
***Bifidobacterium* spp.**	Gram-positive genus in the *Actinobacteria* phylum. Present in breast milk. Colonizes the human GI tract at birth. Common in probiotics. Thrives on a wide variety of prebiotic fibers. Low levels may result from low fiber intake or reduced mucosal health. High levels are more common in children than in adults.
***Enterococcus* spp.**	Gram-positive genus of lactate-producing bacteria in the *Firmicutes* phylum. High levels may be due to reduced digestive capacity, constipation or small intestinal bacterial overgrowth. Low levels may indicate insufficiency of beneficial bacteria.
***Escherichia* spp.**	Gram-negative genus in the *Proteobacteria* phylum. Normal gut flora. *Escherichia coli (E. coli)* is the primary species in this genus. Most *E. coli* are nonpathogenic *(pathogenic E. coli strains are measured separately in "Pathogens" section of the GI-MAP).* High levels may be indicative of increased intestinal inflammatory activity. Low levels may indicate reduced mucosal health and decreased protection against pathogenic *E. coli.*
***Lactobacillus* spp.**	Gram-positive genus of lactate-producing bacteria in the *Firmicutes* phylum. Many strains used as probiotics. High levels may result from reduced digestive capacity or excessive intake of carbohydrates. Low levels may be due to low carbohydrate intake or high salt intake, and may also indicate reduced mucosal health.
***Enterobacter* spp.**	Gram-negative genus in the *Proteobacteria* phylum. Closely related to *E. coli (in the same taxonomic family).* High levels may indicate increased intestinal inflammatory activity. Low levels may indicate reduced mucosal health.
Akkermansia municiphila	Keystone species and primary mucus degrader. Generates mucus-derived sugars and metabolic products that support the growth and energy needs of other gut microbes. Promotes mucosal health and mucus production. Low levels associated with obesity and metabolic dysfunction. High levels linked to multiple sclerosis.
Faecalibacterium prausnitzii	Widely recognized as an important keystone species in the Clostridia class, as well as a major butyrate producer. Promotes anti-inflammatory processes and mucosal homeostasis. Reduced levels have been associated with a wide range of chronic inflammatory and autoimmune diseases.
***Roseburia* spp.**	A genus of Gram-positive anaerobic bacteria in the *Clostridia* class that inhabit the human colon. The *Roseburia* genus has five well-characterized species, all of which produce short chain fatty acids (SCFAs), such as acetate, propionate, and butyrate. *Roseburia* can also produce butyrate from acetate promoting balance in energy homeostasis. The genus is widely recognized to influence colonic motility, support immunity, and suppress inflammation. Low levels are associated with several disease (including irritable bowel syndrome, obesity, Type 2 diabetes, nervous system conditions and allergies).

- **Therapeutic Options for Abnormally Low Commensal Bacterial Findings**
  - » Use a broad-spectrum, diverse probiotic formula, 50–450 billion CFUs/day depending on findings. May contain: *Lactobacillus acidophilus, Bifidobacterium bifidum, Bifidobacterium longum, Lactobacillus rhamnosus, Bifidobacterium breve, Lactobacillus casei, Streptococcus thermophilus.*
  - » Increase dietary intake of vegetables and fibers *(psyllium, oat bran)*
  - » Remove dietary sugar and refined carbohydrates
  - » Prebiotic supplementation *(resistant starch, xylooligosaccharide, inulin, beta-glucan, arabinogalactan)*
  - » Fermented foods, if tolerated
  - » Reduce inflammation and address other imbalances on the GI-MAP
- **Therapeutic Options for Abnormally High Commensal Bacterial Findings**
  - » Consider any additional findings on GI-MAP and treat accordingly
  - » Re-establish commensal bacteria using 5R protocol *(see Table 2)*
  - » Remove dietary sugar and refined carbohydrates
  - » In certain situations, overgrowth of commensal bacteria may be treated judiciously with antimicrobial herbs when all other findings are normal.

FIRMICUTES AND BACTEROIDETES PHYLA

Gram-negative *Bacteroidetes* and gram-positive *Firmicutes* are bacterial phyla that dominate the entire human digestive tract, including the mouth, nose, throat, and colon. An abnormal result in one or both of these phylum suggest imbalanced normal microbes in the GI tract. Further, high *Firmicutes* and low *Bacteroidetes (resulting in a high F/B ratio)* suggest microbial imbalance which may be related to increased caloric extraction from food, fat deposition and lipogenesis, impaired insulin sensitivity, and increased inflammation.

High Firmicutes/Bacteroidetes Ratio

- **Causes:**
  - » Poor diet
  - » Dysbiosis
  - » Maldigestion or hypochlorhydria
- **Therapeutic Approaches & Considerations**
  - » Balance commensal bacteria using the 5R Protocol *(see Table 2)*
  - » When *Firmicutes* phyla is high, consider using *Bifidobacteria* probiotics and *Saccharomyces boulardii* primarily.
  - » *Lactobacillus* spp. and *Bacillus* spp. *(found in probiotics)* can elevate *Firmicutes*
  - » Optimize the diet; a lower fat diet may help to normalize the F/B ratio
  - » Address all other imbalances on the GI-MAP

OPPORTUNISTIC BACTERIA

Many bacteria measured on the GI-MAP are considered opportunistic pathogens, as they only cause disease and illness in some individuals, particularly the immune-compromised. Many individuals come into contact with opportunistic bacteria and experience no symptoms. Most sources consider these microbes to be normal in the stool. However, they can cause gastroenteritis and inflammation at high levels in vulnerable patients. Symptoms may include diarrhea, loose stools, abdominal pain, or even constipation. Overgrowth and excessive colonization by opportunistic bacteria may occur when the commensal bacteria are impaired by poor diet, antibiotic use, parasitic infection, or a weakened immune system. When intestinal permeability is present *(see zonulin)*, these microbes could escape the lumen of the gut and infect extraintestinal sites.

OPPORTUNISTIC/OVERGROWTH MICROBES

Table 8.

DYSBIOTIC & OVERGROWTH BACTERIA	
***Bacillus* spp.**	Common group of gram-positive bacteria in the *Firmicutes* phylum. Some strains are used as probiotics. High levels may result from reduced digestive function, SIBO, or constipation.
Enterococcus faecalis* *Enterococcus faecium	Gram-positive species in the *Firmicutes* phylum. High levels may result from reduced stomach acid, PPI use, compromised digestive function, SIBO or constipation. High natural resistance to some antibiotics, which may result in overgrowth.
***Morganella* spp.**	Gram-negative group in the *Proteobacteria* phylum. May produce histamine. High levels may indicate increased intestinal inflammatory activity. High levels may cause diarrhea, and may also be associated with SIBO.
Pseudomonas* spp.** ***Pseudomonas aeroginosa	Gram-negative bacteria in the *Proteobacteria* phylum. High levels may indicate increased intestinal inflammatory activity and may cause abdominal cramping and loose stools. Some strains of *P. aeroginosa* may produce toxins that can damage cells.
Staphylococcus* spp.** ***Staphylococcus aureus	Gram-positive bacteria in the *Firmicutes* phylum. High levels may result from reduced digestive capacity, and intestinal inflammatory activity. Some strains may produce toxins and contribute to loose stools or diarrhea.
***Streptococcus* spp.**	Gram-positive bacteria in the *Firmicutes* phylum. *Streptococcus* spp. colonize skin and mucous membranes throughout the body; High levels in the intestine may result from low stomach acid, PPI use, reduced digestive capacity, SIBO or constipation; Elevated levels may also be indicative of intestinal inflammatory activity, and may cause loose stools.

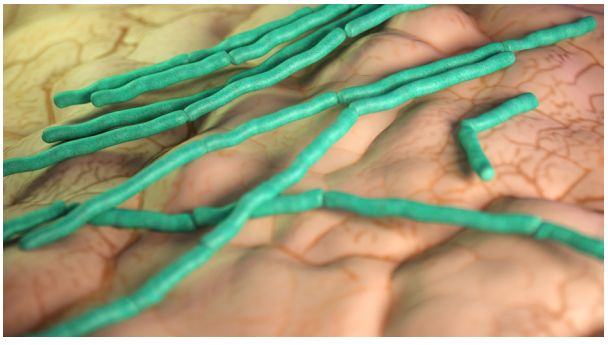
COMMENSAL & OVERGROWTH MICROBES	
***Desulfovibrio* spp.**	A genus of Gram-negative sulfate reducing bacteria. The bacteria produce hydrogen sulfide (H2S), a metabolite which can influence cell signaling and reduce oxidative stress at low concentrations and pose toxicity at higher concentrations.
Methanobacteriaceae (family)	Family of bacteria-like microbes that produce methane. Facilitates carbohydrate fermentation and short-chain fatty acid production by beneficial bacteria. High levels linked to chronic constipation, as well as some types of SIBO and IBS. Low levels may indicate reduced production of short-chain fatty acids and may be associated with inflammation.

INFLAMMATORY & AUTOIMMUNE-RELATED BACTERIA	
***Citrobacter* spp.** ***Citrobacter freundii*.**	Gram-negative bacteria in the *Proteobacteria* phylum. High levels may indicate increased intestinal inflammatory activity.
Klebsiella* spp.** ***Klebsiella pneumoniae	Gram-negative bacteria in the *Proteobacteria* phylum. Common residents of the oral cavity and respiratory tract. May cause diarrhea, gas, abdominal pain, and bloating; Common after long-term antibiotic use; May release histamine in the gut; High levels may indicate increased intestinal inflammatory activity.
Mycobacterium avium subsp. paratuberculosis	Bacterial species in the *Actinobacteria* phylum. Higher levels have been associated with Crohn's disease and rheumatoid arthritis.
Proteus* spp.** ***Proteus mirabilis	Gram-negative bacteria in the *Proteobacteria* phylum. High levels may indicate increased intestinal inflammatory activity; May contribute to loose stools or diarrhea; Pets or wild animals can be a source.

Table 8a.

COMMENSAL INFLAMMATORY & AUTOIMMUNE-RELATED BACTERIA	
***Enterobacter* spp.**	Gram-negative genus in the *Proteobacteria* phylum. Closely related to *E. coli (in the same taxonomic family).* High levels may indicate increased intestinal inflammatory activity. Low levels may indicate reduced mucosal health.
***Escherichia* spp.**	Gram-negative genus in the *Proteobacteria* phylum. Normal gut flora. *Escherichia coli (E. coli)* is the primary species in this genus. Most *E. coli* are nonpathogenic *(pathogenic E. coli strains are measured separately in "Pathogens" section of the GI-MAP).* High levels may be indicative of increased intestinal inflammatory activity. Low levels may indicate reduced mucosal health and decreased protection against pathogenic *E. coli.*
***Fusobacterium* spp.**	Genus of gram-negative bacteria in the *Fusobacteria* phylum. Commonly found in the oral cavity, and may also be found in the intestine. Associated with inflammatory processes, as well as autoimmune conditions such as systemic sclerosis.
***Prevotella* spp.**	Gram-negative species in the *Bacteroidetes* phylum. Associated with rheumatoid arthritis. High levels may result from reduced digestive capacity, or a high-starch diet.

- **Therapeutic Options and Considerations for Abnormally High Levels of Opportunistic Bacteria**
  - » Consider high-dose probiotics (300+ billion CFU/d)
  - » Consider broad-spectrum antimicrobial herbs including: berberine, caprylic acid, garlic oil, oil of oregano, uva ursi, or olive leaf extract
  - » Optimize diet *(low sugar, low refined carbs, high plant-based foods and fiber)*
  - » See SIgA level to determine mucosal immunity and if patient is protected from overgrowth symptoms
  - » Use the 5R Protocol *(see Table 2)*
  - » Identify and remove potential sources of contamination or re-infection
  - » Address all other imbalances on the GI-MAP
  - » If using antibiotics, see the Physician's Desk Reference for appropriate antibiotics for the specific microorganisms that are overgrown
  - » If using antibiotics, consider rifaxamin, which remains in the GI tract and is also used to treat small intestinal bacterial overgrowth (SIBO)



Bacillus cereus

- **Opportunistic Bacteria as a Trigger for Autoimmunity**
  - » Certain opportunistic bacteria may initiate autoimmune thyroiditis or inflammatory arthritis such as rheumatoid arthritis and ankylosing spondylitis. These bacteria may trigger or sustain the autoimmune process. Gastrointestinal symptoms are less common when these bacteria are elevated. When intestinal permeability is present *(see zonulin),* these microbes could escape the lumen of the gut and infect extraintestinal sites.

Table 9. Opportunistic Bacteria and Viruses Associated with Autoimmunity.

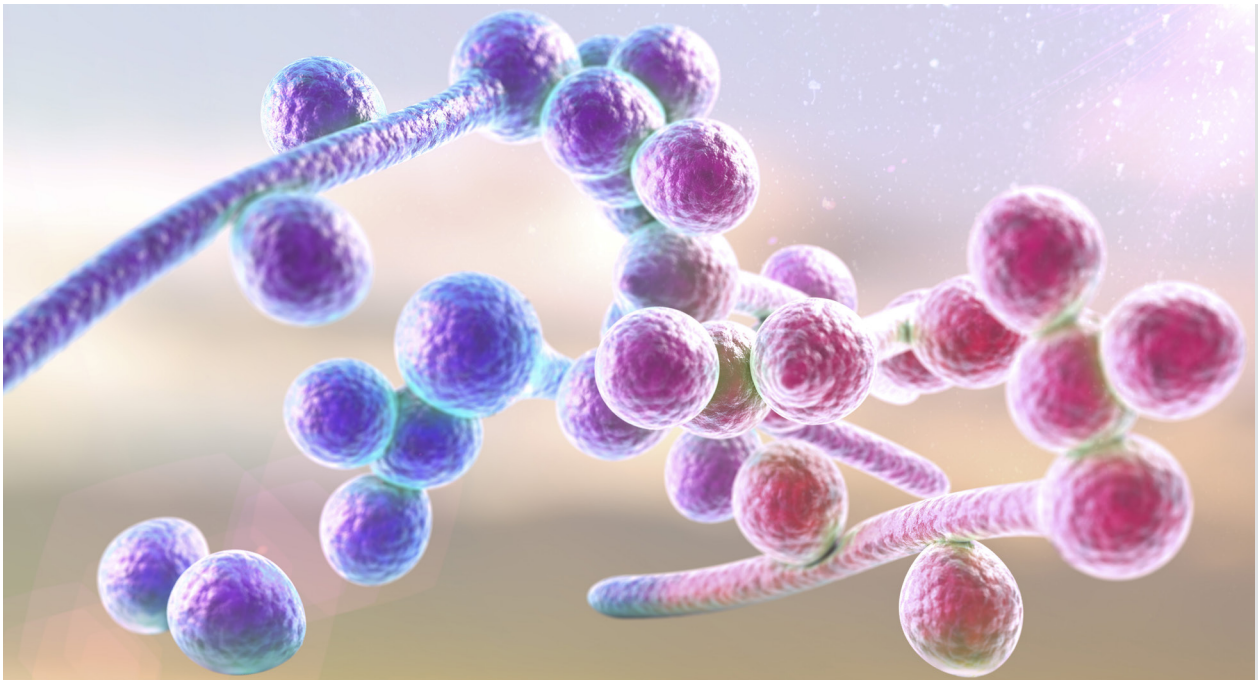
OPPORTUNISTIC BACTERIA AND AUTOIMMUNE ASSOCIATION	
Citrobacter spp.	Rheumatoid arthritis
Fusobacterium spp.	Systemic sclerosis or inflammatory bowel disease
Klebsiella spp.	Crohn's disease, ulcerative colitis, ankylosing spondylitis, and other spondyloarthropathies *(which include ankylosing spondylitis, arthritis associated with Crohn's or ulcerative colitis, psoriatic arthritis, and reactive arthritis)*
M. avium subsp. paratuberculosis	Rheumatoid arthritis, Crohn's disease, Type I diabetes, possibly psoriasis
Prevotella copri	Rheumatoid arthritis
Proteus spp.	Rheumatoid arthritis
Proteus mirabilis	Rheumatoid arthritis and spondyloarthropathies *(listed above)*

VIRUSES AND AUTOIMMUNE ASSOCIATION	
Cytomegalovirus (CMV)	Systemic lupus erythematosus, systemic sclerosis, type 1 diabetes, rheumatoid arthritis
Epstein Barr Virus (EBV)	Rheumatoid arthritis, lupus, Sjogren's, multiple sclerosis, autoimmune thyroid disorders

FUNGI/YEAST

Fungal organisms are commonly found in the human digestive tract, but fungal overgrowth can cause illness in susceptible individuals. Fungal growth may be localized in the body. For instance, *Candida* spp. may be high in the large intestine but normal in the small intestine, and vice versa. In a patient with suspected fungal overgrowth, additional tests may be necessary to understand the complete picture of fungal overgrowth. Urinary D-arabinitol or antibodies to *Candida* are sometimes used.

- **Common Causes of Yeast Overgrowth Include:**
  - » Antibiotic use
  - » High intake of sugar, starches, and dietary fungi *(beer, bread, nuts, cheese, corn)*
  - » Hypochlorhydria
  - » Impaired immune function
  - » Dysbiosis
- **Fungi/Yeast Targeted on the GI-MAP**
  - » *Candida albicans and Candida* spp.
    - – Commensal fungi that can be pathogenic to immunocompromised patients. Causes vaginal yeast infections and can be fatal in systemic infections. May cause diarrhea. Has been suggested to cause a cluster of symptoms including GI complaints, fatigue, and muscle or joint pain but evidence is weak.
  - » *Geotrichum* spp.
    - – May cause disease in immunosuppressed patients. Low levels may be a dietary artefact; certain strains are used to make soft cheeses.
  - » *Microsporidia* spp.
    - – The GI-MAP specifically detects *Encephalitozoon intestinalis,* which affects the GI. May cause diarrhea and wasting. Can disseminate to ocular, genitourinary, and respiratory tracts.



Candida albicans

  - » *Rhodotorula* spp.
    - – Common in soil, plants, bathrooms, and in beverages like milk, juice, and water. May be a commensal. Can cause disease in immunosuppressed patients.

- **Common Symptoms of Fungal Dysbiosis**
  - » GI symptoms: Gas, bloating, constipation, nausea, vomiting, and diarrhea.
  - » Other symptoms: Eczema, athlete's foot, vaginal yeast infections, thrush, and jock itch.

- **Therapeutic Options and Considerations for Abnormally High Levels of Fungi/Yeast**
  - » Reduce intake of sugars, starches, and fungi
  - » See SIgA levels and consider immune support
  - » Consider high-dose probiotics, *Saccharomyces boulardii*, and the 5R Protocol *(see Table 2)*
  - » Consider antifungal herbs such as caprylic acid, undecylenic acid, oregano oil, berberine, and/or garlic
  - » Consider pharmaceutical antifungals in severe cases. Nystatin is preferred because it stays in the GI tract.

VIRUSES

Cytomegalovirus

- **Epidemiology**
  - » Herpes virus that has infected 60% of the US population
  - » One in three children have contracted CMV by five years old
  - » Passed around in child daycare centers
- **Clinical Implications**
  - » Positive CMV on the GI-MAP indicates active infection of the GI, NOT past infection
  - » Active infection may be asymptomatic or cause mild flu-like symptoms
  - » CMV can also cause viral pneumonia, transaminitis, splenomegaly, colitis, fever, and encephalitis
  - » Common in inflammatory bowel disease, immunocompromised patients
  - » CMV colitis has a similar presentation to *Clostridium difficile* infection
  - » CMV has been implicated in autoimmune diseases: lupus, systemic sclerosis, type 1 diabetes, and rheumatoid arthritis

Cytomegalovirus is a viral genus of the viral family known as Herpesviridae

- **Therapeutic Options and Considerations**
  - » No treatment is needed if asymptomatic
  - » Prevent spreading CMV with regular handwashing
  - » Antiviral herbs such as cat's claw, osha root, reishi mushrooms, vitamins A, C, and D, zinc, Echinacea
  - » Address other imbalances on the GI-MAP and use 5R Protocol *(see Table 2)* to rebuild gut health and gut immunity

Epstein Barr Virus

- **Epidemiology**
  - » One of the most common viruses worldwide; infects 90–95% of the population
  - » Commonly contracted in childhood and causes mild symptoms
- **Clinical Implications**
  - » Positive finding on the GI-MAP indicates active EBV infection of the GI, not past infections
  - » Can cause infectious mononucleosis (mono)
  - » Symptoms include fatigue, fever, swollen lymph nodes, inflamed throat, enlarged spleen, and more
  - » May last two to four weeks in adolescents and adults
  - » May cause fatigue for weeks or months
  - » Associated with autoimmune conditions such as rheumatoid arthritis, lupus, Sjogren's, multiple sclerosis, autoimmune thyroid disorders
  - » EBV may increase the risk of gastric cancer; especially if *H. pylori* present
  - » May cause colitis
  - » Found in 30–64% of IBD patients
- **Therapeutic Options and Considerations**
  - » Rest and hydration
  - » Antiviral herbs such as cat's claw, osha root; antiviral fungi such as reishi and/or Cordyceps mushrooms
  - » Vitamins A, C, and D, zinc, Echinacea
  - » Address other imbalances on the GI-MAP and use 5R Protocol *(see Table 2)* to rebuild gut health and gut immunity
  - » Follow-up blood testing may be indicated, including an EBV Early Antigen and EBV PCR test

PARASITES

A parasite is an organism that lives and feeds on a host organism at the expense of the host. The GI-MAP tests for pathogenic parasites and protozoa *(some of which are non-pathogenic)* most commonly occurring in the GI tract. Sources of exposure should be identified and eliminated to prevent reinfection.

PROTOZOA

Blastocystis hominis

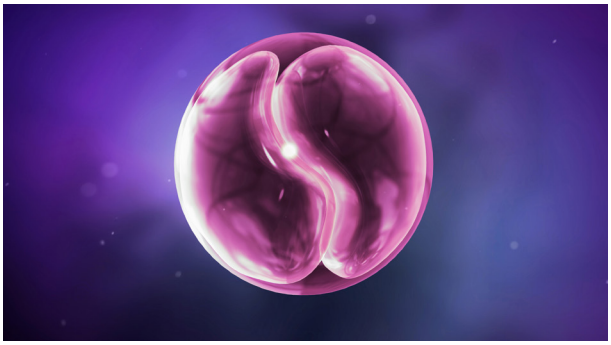
- **Epidemiology**
  - » Fecal contamination of food or water is common
  - » Found worldwide
- **Clinical Implications**
  - » Symptoms include diarrhea, abdominal pain, nausea and vomiting, fever, fatigue, irritable bowel syndrome, infective arthritis
- **Therapeutic options and considerations**
  - » Difficult to eradicate
  - » Consider nitazoxanide or tinidazole, oregano oil, and *S. boulardii*
  - » Herbal treatments may not be as effective
  - » Consider *Artemisia*, *Coptis*, or other broad-spectrum anti-parasitic herbal formulas
  - » Infection can be treated with metronidazole, iodoquinol or trimethoprim/sulfamethoxazole*
  - » Consider probiotics and 5R Protocol *(see Table 2)*

Chilomastix mesnili

- **Epidemiology**
  - » Fecal contamination of food or water
- **Clinical Implications**
  - » Considered non-pathogenic and may not cause symptoms
  - » May indicate dysbiosis or suppressed immunity
- **Therapeutic Options and Considerations**
  - » Look for and address sources of fecal-oral contamination
  - » Consider probiotics and 5R Protocol *(see Table 2)*
  - » Address other imbalances on the GI-MAP

Cyclospora spp. *(Cyclospora cayetanensis)*

- **Epidemiology**
  - » Fecal contamination of food and water
  - » Associated with water- and food-borne outbreaks
  - » Common cause of traveller's diarrhea
  - » May be found on imported fresh produce from tropical regions
- **Clinical Implications**
  - » Symptoms include prolonged watery diarrhea, abdominal cramping, loss of appetite, weight loss, nausea, and vomiting
  - » May cause alternating diarrhea and constipation



Cyclospora

  - » Can cause bloating, flatulence, and burping
  - » Flu-like symptoms such as fatigue, headaches, and low fever may be present in some individuals
  - » Infection is usually self-limiting, with symptoms usually lasting about seven days, but can last weeks or months in immunosuppressed patients
- **Therapeutic Options and Considerations**
  - » In cases lasting more than seven days, treatment with an antibiotic combination of trimethoprim and sulfamethoxazole may be necessary*
  - » Consider probiotics, broad-spectrum anti-parasitic herbal formula, and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of reinfection

Dientamoeba fragilis

- **Epidemiology**
  - » Not well understood; probably fecal contamination of food or water

- **Clinical Implications**
  - » May be asymptomatic
  - » May cause diarrhea, abdominal pain, nausea, fever, fatigue, weight loss, appetite loss, and/or fatigue
- **Therapeutic Options and Considerations**
  - » *"Moderate"* amounts of DNA, that are not above the laboratory reference range, may cause symptoms and warrant treatment
  - » Infection can be treated with iodoquinol, paromomycin, or metronidazole*
  - » Consider probiotics, broad-spectrum anti-parasitic herbal formula, and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of reinfection
  - » Address other imbalances on the GI-MAP

Endolimax nana

- **Epidemiology**
  - » Fecal contamination of food or water
- **Clinical Implications**
  - » Considered non-pathogenic; individuals may be asymptomatic
  - » May be indicative of dysbiosis, conservative treatment may be indicated if clinical presentation is consistent with enteroparasitosis
- **Therapeutic Options and Considerations**
  - » Consider probiotics and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of fecal contamination
  - » Address other imbalances on the GI-MAP

Entameoba coli

- **Epidemiology**
  - » Fecal contamination of food or water
  - » Found in the large intestine, considered to be non-pathogenic
- **Clinical Implications**
  - » May be indicative of dysbiosis, conservative treatment may be indicated if clinical presentation is consistent with enteroparasitosis
- **Therapeutic Options and Considerations**
  - » Consider probiotics and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of fecal contamination
  - » Address other imbalances on the GI-MAP

Pentatrichomonas hominis

- **Epidemiology**
  - » Fecal contamination of food or water
- **Clinical Implications**
  - » Considered harmless, a non-pathogen
  - » Infected individuals are usually asymptomatic
  - » May contribute to dysbiosis
  - » Also colonizes dogs, cats, and other animals

- **Therapeutic Options and Considerations**
  - » May be asymptomatic
  - » In women with vaginosis, consider treatment to reduce chances of vaginal contamination or reinfection *(find treatments for Trichomonas vaginalis elsewhere)*
  - » If treatment is needed, consider a broad-spectrum anti-parasitic herbal formula
  - » Consider probiotics and the 5R Protocol *(see Table 2)*
  - » Look for and address sources of fecal contamination
  - » Address other imbalances on the GI-MAP

WORMS

Ancylostoma duodenale and *Necatur americanus* (Hookworms)

- **Epidemiology**
  - » Infection occurs via skin contact with soil contaminated with larvae or ingestion of larvae
  - » Infected cats and dogs are a source of exposure
  - » *P*revalent in southern Europe, Northern Africa, India, Asia, Caribbean islands, South America, and small areas of the United States
  - » Associated with poor sanitation, inadequate housing construction, and lack of access to medications
- **Clinical Implications**
  - » Early symptoms are itching and rash where the larvae penetrated the skin
  - » Symptoms of heavy infestations include: abdominal pain, diarrhea, fatigue, weight loss, iron deficiency anemia (IDA), coughing, and loss of appetite
  - » Infected individuals may also be asymptomatic
- **Therapeutic Options and Considerations**
  - » Heavy infections can be treated with albendazole or mebendazole*
  - » Individuals presenting with IDA may need iron supplementation
  - » Consider anti-parasitic herbal treatments, gut immunity support, and the 5R Protocol *(see Table 2)*
  - » Look for and remove sources of reinfection

Ascaris lumbricoides (Roundworm)

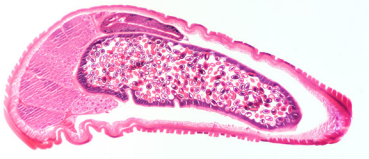
- **Epidemiology**
  - » Fecal contamination of food or water
  - » Common in international travellers and recent immigrants from Latin America and Asia
- **Clinical Implications**
  - » Early symptoms include fever, coughing, wheezing, and dyspnea
  - » Late symptoms include abdominal pain, nausea, vomiting, frequent throat clearing, dry cough, *"tingling throat,"* appendicitis, pancreatitis, and obstruction

» Can cause reactive arthritis

- **Therapeutic Options and Considerations**
  - » Infections may be treated with albendazole, mebendazole, or ivermectin*
  - » Consider anti-parasitic herbal treatments, gut immunity support, and the 5R Protocol *(see Table 2)*
  - » Look for and remove sources of reinfection

Trichuris trichiura (Whipworm)

- **Epidemiology**
  - » Fecal contamination of produce or person-to-person contact
  - » Prevalent in Asia, Africa, South America, and rural southeastern United States
- **Clinical Implications**
  - » Most individuals are asymptomatic, however diarrhea with mucus and blood may occur in some infected individuals
- **Therapeutic Options and Considerations**
  - » Infections may be treated with albendazole, mebendazole, or ivermectin*
  - » Individuals presenting with IDA may need iron supplementation



Microscopic cross section of a whipworm (Thichuris trichiura)

  - » Consider anti-parasitic herbal treatments, gut immunity support, and the 5R Protocol *(see Table 2)*
  - » Look for and remove sources of reinfection

Taenia spp. (Tapeworm)

- **Epidemiology**
  - » Fecal contamination of undercooked pork (*T. solium*) or beef (*T. saginata*)
  - » *T. solium* is found worldwide, but prevalent in communities who raise and eat pigs
  - » *T. saginata* is prevalent in Africa, parts of Eastern Europe, the Philippines, and Latin America where people raise cattle and eat raw beef
- **Clinical Implications**
  - » May be asymptomatic or present with mild symptoms
  - » Symptoms include abdominal pain, nausea, weakness, increased appetite, loss of appetite, headache, constipation, dizziness, diarrhea, pruritus ani, hyperexcitability, and anemia
- **Therapeutic Options and Considerations**
  - » Infections may be treated with albendazole or praziquantel*
  - » Consider anti-parasitic herbal treatments, gut immunity support, and the 5R Protocol *(see Table 2)*
  - » Look for and remove sources of reinfection

INTESTINAL HEALTH MARKERS

DIGESTION

Pancreatic Elastase 1

Elastase 1 is a digestive enzyme secreted exclusively by the pancreas, giving a direct indication of pancreatic function. Elastase 1 is unaffected by pancreatic enzyme replacement therapy.

- **Causes of Low Elastase 1:**
  - » Suppressed pancreatic function
  - » Gallstones
  - » Hypochlorhydria, especially if *H. pylori* present
  - » Cystic fibrosis
  - » Low levels may be found in vegetarians/vegans
- **Common Approaches for Addressing Low Pancreatic Digestive Enzyme Levels:**
  - » Digestive support with betaine HCL
  - » Chew thoroughly and relax at meal time
  - » Pepsin
  - » Plant or pancreatic enzyme supplements
  - » Digestive herbs
  - » Bile salts
  - » Taurine
  - » Consider underlying causes

Table 10. Staging of pancreatic insufficiency based on fecal elastase-1.

Fecal Elastase-1 Result	Clinical Significance
< 200 ug/g	Pancreatic insufficiency
200–500 ug/g	Decreased pancreatic output
> 500 ug/g	Normal pancreatic output

Steatocrit

Fecal fats are normally emulsified by bile salts and absorbed in the small intestines. High levels of fat in the stool may be an indication of maldigestion, malabsorption, or steatorrhea.

- **Causes of Elevated Steatocrit:**
  - » Hypochlorhydria
  - » Maldigestion
  - » Malabsorption
  - » Pancreatic insufficiency *(see elastase-1)*
  - » Bile salt insufficiency
  - » Improper mastication
  - » Celiac disease
- **Therapeutic Approaches and Considerations for High Fecal Fats:**
  - » Support digestion with betaine HCL
  - » Pepsin
  - » Digestive herbs or *"bitters"*
  - » Bile salts
  - » Taurine
  - » Consider underlying causes of malabsorption, such as celiac disease, dysbiosis, or food sensitivities

ADDITIONAL GI MARKERS

Beta-Glucuronidase

High levels of fecal beta-glucuronidase can indicate unfavorable metabolic changes in the colon. Beta-glucuronidase may indicate dysbiosis and interference with Phase II detoxification involving glucuronidation.

- **Major Producers of β-glucuronidase are:**
  - » *Bacteroides fragilis*
  - » *Bacteroides vulgatus*
  - » *Bacteroides uniformis*
  - » *Clostridium paraputrificum*
  - » *Clostridium clostridioforme*
  - » *Clostridium perfringens*
  - » *Escherichia coli*
  - » *Eubacterium*
  - » *Peptostreptococcus*
  - » *Ruminococcus*
  - » *Staphylococcus*
- **Clinical Indications of High β-glucuronidase:**
  - » Dysbiosis in the colon or small intestinal bacterial overgrowth (SIBO)
  - » Extremely elevated cases associated with colon cancer risk
  - » Problems with detoxification, especially estrogen *(via glucuronidation pathway)*
  - » Overexposure to toxins or drugs
- **Therapeutic Approaches and Considerations for Elevated β-glucuronidase:**
  - » Address dysbiosis, if present
  - » Promote bacterial diversity with probiotics, fiber, prebiotics, and fermented foods
  - » Consider liver support such as milk thistle and calcium D-glucarate, especially if patient is taking hormone replacement or has increased cancer risk
  - » If there are no signs of dysbiosis on the GI-MAP, consider a SIBO breath test

Occult Blood Fecal Immunochemical Testing (FIT)

FIT is quantitative and directly measures the concentration of hemoglobin present in stool, rather than just the qualitative presence of hemoglobin. This test uses antibodies specific for human hemoglobin and therefore does not require dietary restrictions or multiple samples, significantly reducing the appearance of false positives. This method has better detection of lower hemoglobin concentrations than qualitative tests, eliminating potential false negatives as well. Literature suggests a result of 10 ug/g may be indicative of potentially more serious conditions such as polyps or colorectal cancer. A variety of ailments can cause lower counts of blood in stool, such as hemorrhoids, anal fissures, pathogenic infection such as giardia, liver disease, and upper GI infections.

- **Possible Causes of Positive Occult Blood:**
  - » Bleeding ulcer
  - » Inflammatory bowel disease
  - » Cancer
  - » Intestinal polyps
  - » Upper GI bleeds that cause iron deficiency anemia
- **Common Approaches for Addressing Fecal Occult Blood**
  - » Identify source
  - » Follow-up testing recommended

IMMUNE RESPONSE

Secretory IgA (SIgA)

Immunoglobulin A is the primary immunoglobulin in the intestinal mucosa. It represents a "first line of defense" in response to antigens and pathogens in the GI and respiratory tracts. In addition to protecting against pathogens, SIgA plays a major role in helping to maintain balance in the microbiome and protecting against exposure to food-derived antigens.

Low Fecal SIgA – The gut immune system is suppressed. Investigate underlying causes, such as chronic dysbiosis, antigen exposure, chronic stress, immunocompromised patient, or even protein malnutrition.

- **Therapeutic Approaches for Low SIgA Levels:**
  - » Address any chronic GI infections, if appropriate
  - » Address microbiome imbalances
  - » Address chronic stress and adrenal health, if needed
  - » Colostrum or immunoglobulins
  - » Supplement with *S. Boulardii*
  - » GI mucosal support with glutamine
  - » Lactobacillus and Bifidobacteria probiotics
  - » General immune support
  - » Essential fatty acids
  - » Zinc
  - » Address other imbalances on the GI-MAP

High Fecal SIgA – Elevated immune response to antigens in the GI tract. Investigate underlying causes, such as chronic dysbiosis, acute infections, acute stress, or food sensitivities.

- **Therapeutic Approaches for High SIgA Levels:**
  - » Address GI infections
  - » Address any food allergies and sensitivities
  - » General immune support

Anti-gliadin SIgA – Gliadin is a component of gluten, the protein found in wheat and other field grass grains such as barley, malt, and rye. The presence of fecal anti-gliadin antibodies can indicate an immune response *(in the gut)* to gluten in the diet. Fecal anti-gliadin antibodies do not necessarily correlate with blood levels.

High Anti-gliadin SIgA – Elevated immune response to gliadin in the lumen of the gut.

- **Treatment:**
  - » Consider gluten elimination for a trial period
  - » If patients have been gluten-free, consider hidden sources of gluten and gliadin cross-reactive food such as dairy, corn, oats, millet, rice and yeast
  - » Consider intestinal barrier support, including supplements such as L-glutamine, zinc carnosine, and colostrum

Eosinophil Activation Protein (EDN/EPX)

EDN/EPX is a protein released by activated eosinophils which has strong cytotoxic characteristics. The protein plays a significant role in a variety of inflammatory and mast-cell mediated pathologies in addition to fighting pathogens, particularly viral infections.

High Eosinophil Activation Protein – The accumulation of eosinophil activation protein in the intestine is associated with inflammation and tissue damage, and the level of EPA in the stool can serve as an objective measure for chronic inflammation in the GI tract. In the case of inflammatory bowel disease, the marker can be used to evaluate disease activity and predict relapse. The EPA marker can also be used to determine the effectiveness of a food elimination diet to control symptoms or disease progression.

- **Possible Causes of Elevated Eosinophil Activation Protein:**
  - » Respiratory allergies
  - » Asthma
  - » Food allergies and sensitivities
  - » IBD
  - » IBS
  - » Eosinophilic esophagitis (EE)
  - » Functional dyspepsia
  - » Acid reflux
  - » Intestinal barrier damage/dysfunction
  - » Anxiety (IBS-related anxiety)
  - » Intestinal parasites

INFLAMMATION

Calprotectin

Fecal calprotectin is the most studied marker of gastrointestinal inflammation. High calprotectin indicates neutrophil infiltration to the gut mucosa. Calprotectin is the gold standard marker for the diagnosis and monitoring of inflammatory bowel disease. It is used to differentiate IBD from irritable bowel syndrome.

- **Possible Causes of Elevated Calprotectin**
  - » Intestinal infections and pro-inflammatory dysbiosis
  - » Food allergens, toxins and certain drugs *(e.g., non-steroidal anti-inflammatory drugs [NSAIDs])*
  - » Inflammatory bowel disease
  - » Polyps
  - » Diverticulitis
  - » Colorectal cancer
- **Therapeutic Approaches and Considerations**
  - » Address possible causes of elevated calprotectin
  - » Persistently elevated calprotectin may indicate chronic inflammatory disease; further evaluation by a qualified medical professional is advised
  - » Consider anti-inflammatory support *(e.g., anti-inflammatory diet, curcumin, omega-3 fatty acids, aloe, and resveratrol)*

ADD-ON TESTS

The following optional add-on tests can be ordered with the GI-MAP.

Zonulin

Zonulin is a protein that opens intercellular tight junctions in the gut lining *(the connections between epithelial cells that make up the gastrointestinal lining).* Zonulin increases intestinal permeability in the jejunum and ileum and is considered a biomarker for barrier permeability.

- **Therapeutic Approach for Elevated Intestinal Permeability:**
  - » Address dysbiosis *(pathogens and opportunistic microbe overgrowth, lack of beneficial microbes)*
  - » Eliminate gluten, address potential food sensitivities
  - » Promote a healthy intestinal barrier with L-glutamine, butyrate, essential fatty acids, aloe vera, probiotics, zinc carnosine, slippery elm, marshmallow, deglycyrrhizinated licorice

Zonulin is available as an optional add-on to the GI-MAP, or as a stand-alone test.

Gluten Peptide

The Gluten Peptide test detects the presence of gluten in stool. Gluten is broken into gliadin and glutenin subunits during the digestive process. A specific section of the gliadin protein, referred to as the 33-mer peptide,* is resistant to digestion in the human gastrointestinal (GI) tract but can be accurately detected in stool several days after the consumption of gluten.

The Gluten Peptide test can help practitioners monitor a patient's gluten-free (GF) diet compliance. Any detected level of the fecal gluten protein indicates dietary exposure to gluten within the previous 2–4 days.†

- **Clinical Implications:**
  - » For patients following a GF diet, detected levels of the gluten peptide can indicate accidental exposure from hidden sources or food cross-contamination
  - » For patients regularly consuming gluten, detected levels are expected findings

The Gluten Peptide marker is available as an optional add-on to the GI-MAP, or as a stand-alone test.

* *Because of structural homology (the structural similarity) of gluten proteins, detected 33-mer gliadin protein may indicate the consumption of wheat, rye, barley, corn, or oat grain.*

† *Speed of digestion (motility and transit time) can influence the transience of gluten peptide in stool.*

Universal Antibiotic Resistance (AR) Genes Panel

The Universal Antibiotic Resistance Genes Panel detects the presence of 55 genetic elements associated with resistance to 10 different classes of antibiotics. Useful for patients who have been hospitalized, treated with antibiotics, or who have stubborn, chronic infections, the Universal Antibotic Resistance Genes panel can inform practitioners if antibiotic resistance is a potential stumbling block for patients.

The Universal Antibiotic Resistance (AR) Gene Panel is available as an optional add-on only to the GI-MAP, or Pathogens Panel. See page 42 for more information regarding AR Genes testing on the GI-MAP and antibiotic stewardship.

StoolOMX™

StoolOMX measures gut microbial metabolites that evaluate 25 bile acids and 9 short chain fatty acids, providing actionable insights into conditions like IBS, IBD, and bile acid diarrhea.

StoolOMX is available as an optional add-on to the GI-MAP. Please see StoolOMX on page 44 for a detailed interpretive overview.

ANTIBIOTIC RESISTANCE GENES

In an effort to promote antibiotic stewardship, the GI-MAP **includes** results of ***H. pylori Antibiotic Resistance Genes*** in the microbiome as part of the test. Additionally, the ***Universal Antibiotic (AR) Resistance Genes*** panel can be ordered as an **add-on** to the GI-MAP or to the GI-Pathogens panel.

Antibiotic Stewardship

Antibiotic stewardship is the effort to measure and improve how antibiotics are prescribed by clinicians and used by patients. If an antibiotic resistance gene is present, then that class of antibiotics is designated POSITIVE for antibiotic resistance. A positive result for the presence of resistance genes for a given antibiotic indicates that the antibiotic is not an ideal choice for an antibiotic protocol.

H. pylori Antibiotic Resistance Genes

The *H. pylori* Antibiotic Resistance Genes are specific to the *H. pylori* genome detected on an individuals' GI-MAP. These results will only be reported if the *H. pylori* result is 5.0e2 or greater.

Universal Antibiotic Resistance Genes

The Universal Antibiotic resistance genes apply to *all* of the microorganisms within the fecal sample. Since microbes can rapidly share DNA under stress, the presence of antibiotic resistance in any organism is reason enough to avoid that drug class.

H. PYLORI ANTIBIOTIC RESISTANCE GENES

	Result	Reference
Amoxicillin	**Positive**	**Negative**
Genes associated with amoxicillin resistance		
PBP1A S414R	**Present**	
PBP1A T556S	**Absent**	
PBP1A N562Y	**Absent**	

	Result	Reference
Clarithromycin	**Positive**	**Negative**
Genes associated with clarithromycin resistance		
A2142C	**Absent**	
A2142G	**Absent**	
A2143G	**Present**	

	Result	Reference
Fluoroquinolones	**Negative**	**Negative**
Genes associated with fluoroquinolone resistance		
gyrA N87K	**Absent**	
gyrA D91N	**Absent**	
gyrA D91G	**Absent**	
gyrB S479N	**Absent**	
gyrB R484K	**Absent**	

	Result	Reference
Tetracycline	**Negative**	**Negative**
Genes associated with tetracycline resistance		
A926G	**Absent**	
AGA926-928TTC	**Absent**	

Figure 4. Sample *H. pylori* Antibiotic Resistance Genes Section. *See additional details in the "Helicobacter pylori" section of this guide (Page 17, Figure 2).*

UNIVERSAL ANTIBIOTIC RESISTANCE GENES

	Result	Reference
b-Lactams	**Negative**	**Negative**
blaNDM-1	**Absent**	
CTX-M 1	**Absent**	
CTX-M 2	**Absent**	
CTX-M 8/25	**Absent**	
CTX-M 9	**Absent**	
GES	**Absent**	
OXA-1	**Absent**	
PER-1	**Absent**	
PER-2	**Absent**	
SHV	**Absent**	
TEM	**Absent**	
VEB	**Absent**	
Fluoroquinolones	**Positive**	**Negative**
qnrA	**Present**	
qnrB	**Absent**	
qnrS1	**Absent**	
Vancomycin	**Negative**	**Negative**
vanA	**Absent**	
vanA2	**Absent**	
vanB	**Absent**	
vanC1	**Absent**	
vanC2-1	**Absent**	
vanC2-2	**Absent**	

	Result	Reference
Macrolides	**Negative**	**Negative**
acrA	**Absent**	
acrB	**Absent**	
emrE	**Absent**	
ermA	**Absent**	
ermB	**Absent**	
ermC	**Absent**	
macA	**Absent**	
macB	**Absent**	
mefA	**Absent**	
mphA	**Absent**	
msrA	**Absent**	
tolc	**Absent**	
Ciprofloxacin	**Negative**	**Negative**
emea	**Absent**	
pmra	**Absent**	
Nitroimidazoles	**Negative**	**Negative**
nimA	**Absent**	
nimB	**Absent**	
nimC	**Absent**	
nimD	**Absent**	
nimE	**Absent**	

	Result	Reference
Trimethoprim	**Negative**	**Negative**
dfrA1	**Absent**	
dfrA12	**Absent**	
dfrA14	**Absent**	
dfrA15	**Absent**	
dfrA17	**Absent**	
dfrA5	**Absent**	
dfrA7	**Absent**	
dfrB1	**Absent**	
dfrB2	**Absent**	
dfrB3	**Absent**	
Sulfonamides	**Positive**	**Negative**
sul1	**Present**	
sul2	**Present**	
sul3	**Present**	
Methacillin	**Negative**	**Negative**
mecA	**Absent**	
Chloramphenicol	**Negative**	**Negative**
cata13	**Absent**	

Figure 5. Sample Universal Antibiotic Resistance Genes Panel. *Available as an optional add-on only to the GI-MAP, or Pathogens Panel.*

StoolOMX™

StoolOMX measures gut microbial metabolites—a comprehensive set of bile acids (BA) and short chain fatty acids (SCFA) via LC-MS/MS. This data offers an in-depth understanding of the stool metabolome and its clinical applications. The StoolOMX profile can be ordered as an **add-on** to the GI-MAP.

BILE ACIDS

Primary bile acids are natural products produced in the liver from cholesterol synthesis. These primary bile acids are conjugated with either taurine or glycine to increase solubility and are stored in the gallbladder as bile.

Primary, conjugated bile acids are the main component in bile. At mealtime, they aid in the emulsification and absorption of dietary fats in the small intestine. After contributing to fat absorption, the majority (~95%) of primary bile acids are reabsorbed in the distal ileum and returned to the liver via the portal vein—a process called enterohepatic circulation. A small portion (~5%) of primary bile acids will reach the colon, where they are metabolized by gut bacteria and deconjugated (glycine and taurine removed) to produce unconjugated secondary bile acids. Deconjugation is generally favorable.

Commensal gut bacteria deconjugate bile acids to facilitate their reabsorption and recycling while also preparing them for further bacterial modification.

Under normal physiological conditions, most bile acids are reabsorbed, and very few bile acids are excreted in stool. Under abnormal physiological conditions, excess bile acids enter the colon and can promote inflammation and diarrheal symptoms while exerting negative effects on commensal bacteria.

Measuring concentrations and ratios of bile acids in stool can offer root-cause insights into digestive symptoms, malabsorptive disorders, immune system regulation, and even metabolic impacts. Furthermore, altered patterns of bile acid metabolites have emerging disease state associations and can be used as part of diagnostic workup and treatment management in conditions such as bile acid diarrhea (BAD), inflammatory bowel disease (IBD), and irritable bowel syndrome (IBS) (-C, -D, -M).

StoolOMX measures 25 bile acid metabolites in total concentrations, percents, and ratios. This data offers an in-depth understanding of the stool metabolome and impactful clinical considerations.

BILE ACIDS – SUMMARY

Total Bile Acids Concentration

- **An absolute concentration of total bile acids in stool measured in ng/g**
  - » Reflects the amount of bile acids reaching the colon and not reabsorbed in the distal ileum after digestion
- **Elevated Total Bile Acids:**
  - » Excess/elevated bile acids in stool is an indication of bile acid malabsorption (BAM) and often results in symptoms such as diarrhea (bile acid diarrhea – BAD)
  - » Quantification of bile acids may be part of a comprehensive workup for irritable bowel syndrome with diarrhea (IBS-D), as it is currently estimated that up to 1/3 of IBS-D patients present with BAD
  - » Elevated stool bile acids may suggest altered bile acid production or reabsorption, which could be due to liver disease, gallbladder dysfunction, intestinal issues, or diet composition
- **Low Total Bile Acids:**
  - » Low total bile acid concentrations in stool are generally favorable but may be indicative of slow transit or constipation

Total Primary Bile Acids Percent

- **Percent concentration of primary bile acids in stool**
  - » Primary bile acids should be present in very low concentrations in stool
  - » Primary bile acids in the colon can be damaging to the gut lining and can have antimicrobial action on the microbiome
  - » Higher levels of primary bile acids in a stool sample are indicative of excess production or BAM and are associated with an array of GI symptoms and disease states, including IBD
  - » See individual primary bile acid concentrations on page 2 of the StoolOMX report for further analysis and associations

Total Secondary Bile Acids Percent

- **Inverse of total primary bile acids in stool**
  - » Listed as percent concentration of secondary bile acids in stool
  - » Secondary bile acids should be present in high concentrations in stool
  - » Secondary bile acids play diverse roles in regulating intestinal motility, gut barrier function, metabolism, and immune balance
  - » In general, a higher number of secondary bile acids relate to a healthier, more diverse microbiome and normal physiological GI function
  - » See individual secondary bile acid concentrations on page 2 of the StoolOMX report for further analysis and associations

Table 11. This section represents the most abundant bile acids.

PERCENTAGE BREAKDOWN OF MOST ABUNDANT BILE ACIDS		
SECONDARY BILE ACIDS	**FUNCTION**	**AVERAGE PERCENTAGE†**
Deoxycholic Acid (DCA)	DCA is a major secondary bile acid that is formed from the bacterial metabolism of CA. Low levels observed in ulcerative colitis (UC). Elevated levels are associated with liver and colon cancer and metabolic imbalance. Implicated in modulating the immune response by inhibiting pro-inflammatory cytokine production. Can inhibit *Lactobacillus* spp., *Bifidobacterium* spp., and *Bacteroides fragilis*.	**48%**
Lithocholic Acid (LCA)*	LCA is a major secondary bile acid that is formed from the bacterial metabolism of CDCA. Low levels observed in UC. Elevated levels are associated with liver and colon cancer and may contribute to blood sugar dysregulation. Modulates immune responses at normal levels.	**27%**
Isolithocholic Acid (Iso-LCA)	Prevalent secondary bile acid in stool that has positive associations with longevity. Influences metabolic health, interacts with cellular receptors, and modulates immune responses at normal levels. Influences the differentiation and function of T cells, particularly T helper 17 (Th17) cells, which play a critical role in the inflammatory response.	**8%**
Other	The remaining primary and secondary bile acid metabolites measured on StoolOMX.	**17%**

** On StoolOMX, the LCA value is a summation of LCA + Allo-LCA.; † Reference set at 50th percentile.*

LCA/DCA Ratio

LCA and DCA are secondary bile acids formed from CDCA and CA in the colon. CDCA is converted to LCA, and CA is converted to DCA. This ratio can be useful in determining the risk of certain disease states and conditions.

LCA is thought to be more toxic than DCA due to its inhibitory effects on antioxidant pathways. An elevated ratio can be seen in patients with gallstones and after cholecystectomy. A higher ratio is also associated with an increased risk for colon cancers, while a lower ratio may indicate a reduced cancer risk.

Bile Acids: Therapeutic Applications

Bile acids and the microbiome have a bidirectional relationship and impact. It is important to first evaluate patient symptoms, such as stool frequency and Bristol stool type.

Always analyze StoolOMX results with GI-MAP findings and support accordingly. It is important to assess liver function, as bile acids are originally produced in the liver.

If there are significant imbalances in the bile acids summary, review the list of individual bile acids on page 2 of the StoolOMX report.

- **A healthy microbiome is typically associated with:**
  - » Total bile acid concentration in normal range
  - » High secondary bile acid percent
- **An unhealthy microbiome is typically associated with:**
  - » Elevated total bile acid concentration
  - » High primary bile acid percent, as the microbiome is responsible for converting primary bile acids to secondary bile acids
- **Common GI-MAP patterns that may be associated with abnormal StoolOMX results:**
  - » Presence of pathogens
  - » Insufficiency dysbiosis
  - » Increased *Firmicutes:Bacteroidetes* ratio
  - » Overgrowth of GI-MAP (report page 3) inflammatory opportunists
  - » Elevated Steatocrit
  - » Decreased Elastase-1
  - » Elevated Calprotectin
- **Lifestyle Considerations**
  - » Evaluate macronutrient composition of diet with respect to calories from fat. Patients may need to adopt a lower fat diet if StoolOMX results are abnormal.
  - » Evaluate and ensure adequate dietary fibers
  - » Anti-inflammatory dietary practices
  - » Support liver and gallbladder
  - » Incorporate regular exercise
- **Medication/Supplement Considerations for BAM**
  - » Bile acid sequestrants
    - – ex: cholestyramine, colesevelam
  - » Tauroursodeoxycholic acid (TUDCA)
  - » Digestive support as needed
    - – Digestive enzymes, betaine HCL, digestive bitters, ox bile, etc.
  - » Activated charcoal
  - » Pectin fibers
  - » Probiotics
  - » Polyphenols such as resveratrol

Table 12. GI-MAP microbes involved in deconjugation of primary bile acids to secondary bile acids.

GI-MAP MICROBES
***Firmicutes* phyla**
***Bacteroidetes* phyla**
***Escherichia* spp.**
***Bacteroides* spp.**
***Bifidobacterium* spp.**
***Enterococcus* spp.**
***Lactobacillus* spp.**
***Methanobacteriaceae* family**

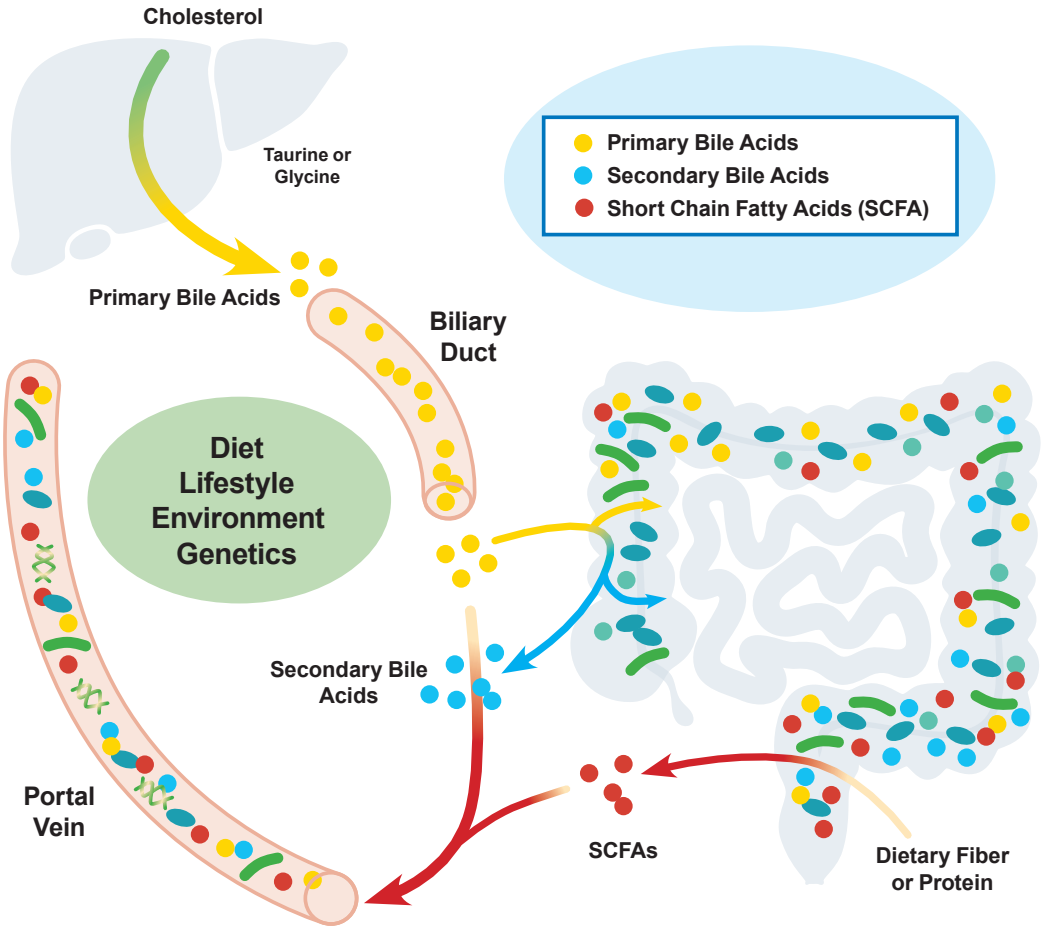


Figure 6. Bile Acids and Fatty Acids Overview.

Primary bile acids are synthesized from cholesterol in the liver and conjugated with either taurine or glycine. They are stored in the gallbladder and released during digestion to assist with the absorption of fat and fat-soluble vitamins. Normally, ~95% of primary bile acids are reabsorbed via the portal vein, while ~5% are metabolized by gut bacteria to produce secondary bile acids.

Saccharolytic short chain fatty acids (SCFAs) are primarily metabolites of dietary fiber fermentation in the gut while proteolytic branched chain fatty acids (BCFAs) are metabolites of protein fermentation. Acetate, propionate, and butyrate are three major SCFAs, which account for ~90% of the SCFAs produced by gut microbiota. SCFAs are known to have numerous health effects and can enhance fecal excretion of bile acids.

SHORT CHAIN FATTY ACIDS – SUMMARY

Short chain fatty acids (SCFAs) are small (0-6 carbon) saturated fatty acids that are produced from the microbiome (gut bacteria) by fermentation of food substrates. Fermentation of carbohydrate—called saccharolytic fermentation—produces straight chain fatty acids (SCFA). Fermentation of protein—called proteolytic fermentation—produces branched chain fatty acids (BCFA).

StoolOMX measures 9 short chain fatty acid metabolites in percentages, total concentrations, and ratios. The test also includes the ratio of straight chain fatty acids to branched chain fatty acids. Ratios can provide insight into dietary composition and digestive impacts such as saccharolytic and proteolytic (putrefactive) fermentation and digestive insufficiency. Assessing SCFA levels in stool offers a deeper look into digestive health and the overall balance of the gut microbiome.

Major SCFAs

Acetate, butyrate, propionate, and valerate are the major primary straight chain metabolites. As preferred fuel for intestinal cells, these metabolites provide a variety of beneficial effects for intestinal health.

SCFAs serve as an energy source for colon cells, strengthen the gut barrier and provide metabolic and immune system signaling. They have a profound anti-inflammatory effect by inducing and selectively expanding T-regulatory cells (T regs) in the large intestine, which, in turn, suppresses the pro-inflammatory action of Th17. As metabolites of bacterial fermentation, their levels can reflect gut microbiota composition.

Low levels of SCFAs are linked to various conditions, including irritable bowel syndrome, obesity, and inflammatory bowel disease. Low levels may also be related to slow motility.

Table 13.

PERCENT BREAKDOWN OF MAJOR SHORT CHAIN FATTY ACIDS REPRESENTED ON STOOLOMX		
MAJOR SCFA	FUNCTION	AVERAGE PERCENTAGE†
Acetate	Most abundant SCFA. Involved in lipid synthesis and appetite regulation, maintains energy balance and metabolic homeostasis. Resists oxidation and mitochondrial stress.	**52%**
Butyrate	Primary energy source for colonic cells. Supports intestinal barrier integrity, reduces intestinal inflammation, promotes motility, enhances fatty acid oxidation, inhibits tumor cell progression, and fosters a balanced microbiome.	**20%**
Propionate	Supports intestinal barrier integrity, impacts energy balance, gluconeogenesis, and lipid metabolism. Involved in appetite regulation. Proposed as a biomarker for IBS.	**25%**
Valerate	Stimulates intestinal epithelium growth, inhibits colon cancer cell production, modulates glucose and lipid metabolism. Antimicrobial effects against *C. difficile*.	**3%**

† Reference set at 50th percentile.

SCFA/BCFA Ratio

Saccharolytic straight chain fatty acids (SCFAs) are primary metabolites of dietary fiber fermentation in the gut while proteolytic branched chain fatty acids (BCFAs) are metabolites of protein fermentation.

Ideally, saccharolytic SCFAs should make up ~95% of total SCFAs, while BCFAs should make up ~5% of total SCFAs.

The production of branched chain fatty acids leads to other fermentation products that can be harmful to the colon epithelium, such as ammonia, phenol, p-cresol, or biogenic amines. BCFAs are mainly produced during fermentation of branched chain amino acids (valine, leucine, and isoleucine) by the intestinal microbiota.

High levels of BCFAs compared to saccharolytic SCFAs can indicate weak digestion, poor transit, and inflammatory dysbiosis. There may also be associations between elevated BCFA concentrations in stool and obesity, IBD, hypercholesterolemia, and metabolic-associated fatty liver disease (MAFLD).

The SCFA/BCFA ratio may decline with age, primarily due to a significant decrease in SCFA levels in stool.

Short Chain Fatty Acids: Therapeutic Applications

- **Causes for Low SCFA Levels:**
  - » Diarrhea (rapid transit leading to decreased SCFA production)
  - » Constipation (slow transit leading to increased SCFA absorption)
  - » Inflammation (high calprotectin)
  - » Chronic antibiotic use
  - » Low complex carbohydrate and fiber intake
  - » Insufficiency dysbiosis
  - » Inflammatory bowel disease
- **Cause for High SCFA Levels:**
  - » Increased transit time (diarrhea)
- **Causes for High BCFA Levels:**
  - » High protein intake and low fiber and/or polyphenol intake (Western diet)
  - » Low total SCFAs
  - » Weak digestion/hypochlorhydria
  - » Increased age
  - » Metabolic imbalance
- **Therapeutic Options and Considerations to Increase Levels of SCFAs:**
  - » Ensure diet is high and diverse in plant-based fibers, polyphenols, and fermented foods
  - » Avoid antibiotics
  - » Consider probiotics to support butyrate-producing organisms
  - » Consider support with butyrate salts
  - » Intestinal barrier support
  - » Support digestion if indicated
  - » Maintain a healthy weight

Table 14. The bacteria involved in the production of saccharolytic straight chain fatty acids and proteolytic branched chain fatty acids. Acetate, propionate, and butyrate make up ~90–95% of fecal SCFAs, with valerate and caproate comprising a smaller percentage. Isobutyrate, isovalerate, 2-methylbutyrate, and isocaproate make up ~5–10% of fecal SCFAs. Microbiota listed below each metabolite are involved in the production of that respective fatty acid.

BACTERIA INVOLVED IN SHORT CHAIN FATTY ACID PRODUCTION			
	SACCHAROLYTIC STRAIGHT CHAIN FATTY ACIDS (SCFA)	PROTEOLYTIC BRANCHED CHAIN FATTY ACIDS (BCFA)	
~90–95 Percent of Fecal SCFAs	**Acetate** • *Blautia hydrogenotrophica* • *Bifidobacterium* spp. • *Lactobacillus* spp. • *Clostridium* spp. • *Streptococcus* spp.	**Isobutyrate** • *Bacteroides* spp. • *Clostridium* spp.	~5–10 Percent of Fecal SCFAs
	Propionate • *Bacteroidetes* • *Negativicutes* • *Megasphaera elsdenii* • *Lachnospiraceae* • *Coprococcus catus* • *Akermansia municiphilia*	**Isovalerate** • *Bacteroides* spp. • *Clostridium* spp.	
	Butyrate • *Firmicutes* phyla • *Faecalibacterium prausnitzii* • *Roseburia* spp. • *Eubacterium* spp. • *Clostridium coccoides*	**2-Methylbutyrate** (from leucine) • *Bacteroides* spp. • *Clostridium* spp.	
	Valerate (potentially toxic) • *Clostridia*	**Isocaproate** (associated with disease)	
	Caproate (potentially toxic – from lactate) • *Megasphaera elsdenii* • *Clostridium* spp. BS-1		

- **Therapeutic Options and Considerations to Decrease Levels of SCFAs:**
  - » Low-FODMAP diet
  - » Maintain a healthy weight
  - » Support digestion if indicated
  - » Consider multi-strain probiotics to decrease acetate concentrations

- **Therapeutic Options and Considerations to Decrease Levels of BCFAs:**
  - » Increase fiber intake (particularly insoluble fibers) and/or decrease protein intake
  - » Consider underlying associations such as inflammatory bowel disease, chronic kidney disease, obesity, type 2 diabetes mellitus, MAFLD, or impaired digestion

INDIVIDUAL BILE ACID RESULTS

Research is more widely available on the clinical implications of certain primary and secondary bile acids compared to others.

Table 15.

PRIMARY BILE ACIDS		
MARKER	ABBR	GUIDE
Cholic Acid	**CA**	Major primary bile acid. May be increased in IBS-D patients. CA levels in stool may serve as a biomarker for IBS and UC. During a UC flare, deconjugation of CA to DCA may be impaired. Can inhibit *Roseburia* spp. and *Lactobacillus* spp.
Chenodeoxycholic Acid	**CDCA**	Major primary bile acid. May be increased in IBS-D patients and may contribute to visceral hypersensitivity. Elevated levels may be associated with metabolic imbalance.
Taurochenodeoxycholic Acid	TCDCA	Minor primary bile acid.
Taurocholic Acid	TCA	A whole grain diet may increase levels of TCA.
Glycochenodeoxycholic Acid	GCDCA	May be increased in IBS-D patients.
Glycocholic Acid	GCA	A whole grain diet may increase levels of GCA.
Hyocholic Acid	HCA	Lower levels are associated with pre-diabetes. HCA levels may serve as an indication of metabolic health.

Table 16.

SECONDARY BILE ACIDS		
MARKER	ABBR	GUIDE
Lithocholic Acid*	**LCA**	LCA is a major secondary bile acid that is formed from the bacterial metabolism of CDCA. Low levels observed in UC. Elevated levels are associated with liver and colon cancer and may contribute to blood sugar dysregulation. Modulates immune responses at normal levels.
Deoxycholic Acid	**DCA**	DCA is a major secondary bile acid that is formed from the bacterial metabolism of CA. Low levels observed in ulcerative colitis (UC). Elevated levels are associated with liver and colon cancer and metabolic imbalance. Implicated in modulating the immune response by inhibiting pro-inflammatory cytokine production. Can inhibit *Lactobacillus* spp., *Bifidobacterium* spp., *Bacteroides fragilis,* and *Clostridium difficile*.
Isolithocholic Acid	**Iso-LCA**	Prevalent secondary bile acid in stool that has positive associations with longevity. Influences metabolic health, interacts with cellular receptors, and modulates immune responses at normal levels. Influences the differentiation and function of T cells, particularly T helper 17 (Th17) cells, which play a critical role in the inflammatory response.

Table 16. *Continued.*

SECONDARY BILE ACIDS		
MARKER	ABBR	GUIDE
12-Ketolithocholic Acid	12-KLCA	Prevalent secondary bile acid in stool. May provide anti-inflammatory effects in IBD, modulate cholesterol metabolism, and improve glucose homeostasis.
3-oxoDeoxycholic Acid	3-oxoDCA	Prevalent secondary bile acid in stool that has positive associations with longevity.
Ursodeoxycholic Acid	UDCA	Enhances bile flow, hepatoprotective, and has immunomodulatory properties. Levels in stool may serve as a biomarker of IBS and UC. Elevated levels may be associated with metabolic imbalance.
Glycolithocholic Acid	GLCA	May be negatively correlated with fecal calprotectin levels in UC. Influences metabolic signaling pathways, modulates gut microbiome, involved in lipid absorption, and aids in the detoxification of potentially harmful bile acids.
Glycoursodeoxycholic Acid	GUDCA	Modulates the gut microbiome, cytoprotective, and influences lipid and glucose metabolism. May be elevated in IBS-D.
Glycodeoxycholic Acid	GDCA	Modulates the gut microbiome. Involved in lipid absorption and metabolic regulation. May be reduced in UC.
Taurolithocholic Acid	TLCA	Involved in lipid absorption and metabolic regulation. Modulates inflammation and may exert cholestatic effects when dysregulated. A whole grain diet may increase levels of TLCA.
Tauroursodeoxycholic Acid	TUDCA	Often used synthetically as a supplement. Used clinically for cholestatic liver diseases. Cytoprotective, particularly in the liver. Involved in the regulation of bile acid metabolism and lipid metabolism. Neuroprotective and modulates inflammation.
Taurodeoxycholic Acid	TDCA	Involved in bile acid metabolism and lipid metabolism. Modulates the gut microbiome and has anti-inflammatory properties.
7-Ketolithocholic Acid	7-KLCA	Involved in bile acid metabolism and cholesterol metabolism. Modulates the gut microbiome.
Dehydrolithocholic Acid	DHLCA	Involved in bile acid metabolism and modulation of the gut microbiome. Exerts anti-inflammatory properties.
Hyodeoxycholic Acid	HDCA	May be negatively correlated with fecal calprotectin levels in UC. May have anti-atherosclerotic effects. Involved in lipid absorption and cholesterol metabolism. Modulates the gut microbiome.
Alloisolithocholic Acid	AlloIso-LCA	Positive associations with longevity and exerts antibacterial effects against gram-positive pathogens.
3-Dehydrocholic Acid	3-DHCA	Involved in bile acid metabolism and exerts anti-inflammatory properties.

** On StoolOMX, the LCA value is a summation of LCA + Allo-LCA.*

INDIVIDUAL SHORT CHAIN FATTY ACIDS RESULTS

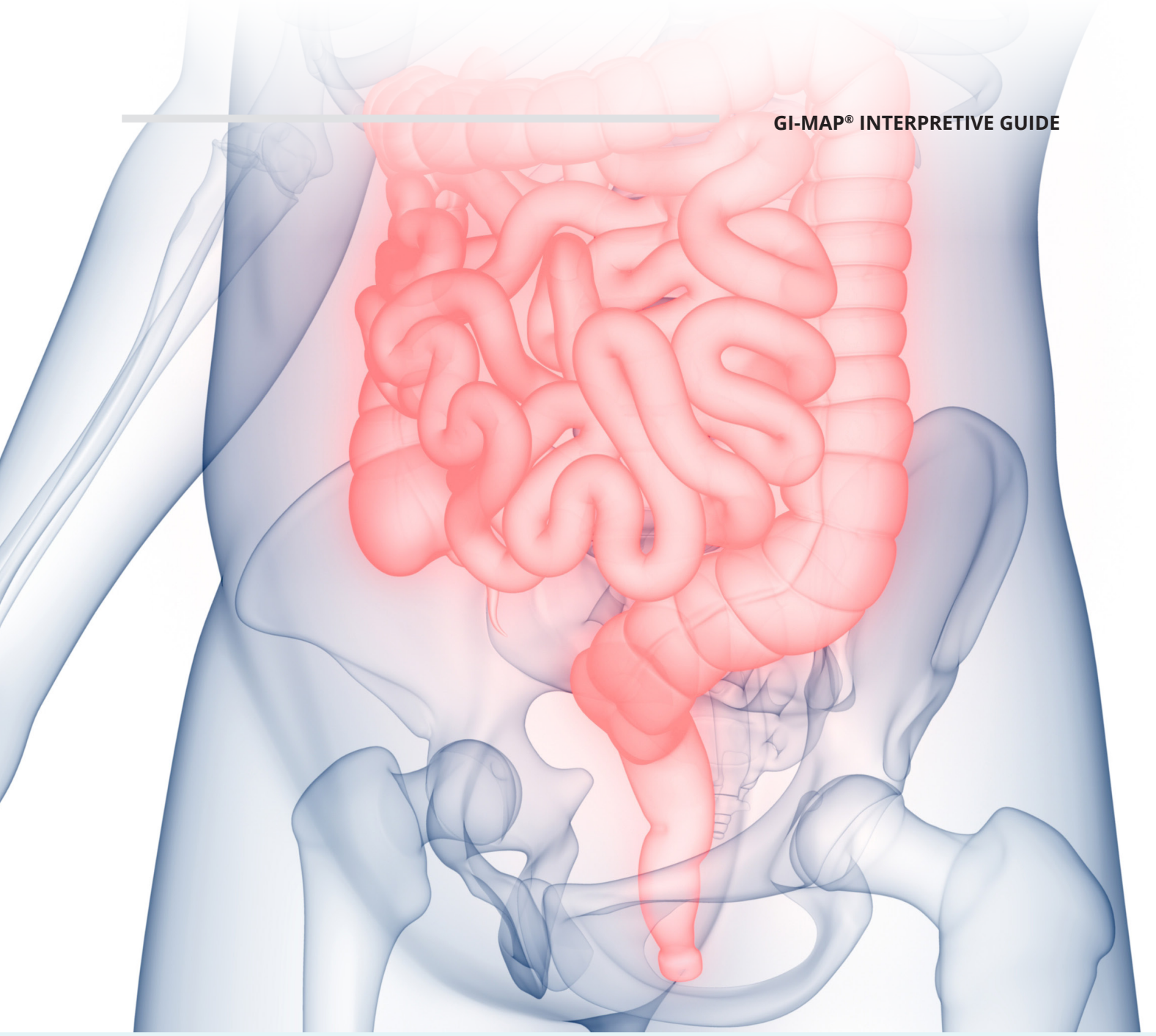
Table 17.

SACCHAROLYTIC STRAIGHT CHAIN FATTY ACIDS (SCFA)	
MARKER	**GUIDE**
Acetate	Most abundant SCFA. Involved in lipid synthesis and appetite regulation, maintains energy balance and metabolic homeostasis. Resists oxidation and mitochondrial stress.
Butyrate	Primary energy source for colonic cells. Supports intestinal barrier integrity, reduces intestinal inflammation, promotes motility, enhances fatty acid oxidation, inhibits tumor cell progression, and fosters a balanced microbiome.
Propionate	Supports intestinal barrier integrity, impacts energy balance, gluconeogenesis, and lipid metabolism. Involved in appetite regulation. Proposed as a biomarker for IBS.
Valerate	Stimulates intestinal epithelium growth, inhibits colon cancer cell production, modulates glucose and lipid metabolism. Antimicrobial effects against *C. difficile*.
Caproate	Antimicrobial effects against *C. difficile*.

PROTEOLYTIC BRANCHED CHAIN FATTY ACIDS (BCFA)	
MARKER	**GUIDE**
Isobutyrate	Stimulates colonic sodium absorption. Elevated levels in stool may be associated with cortisol levels and depression.
Isovalerate	Elevated levels in stool may be associated with depression by its influence on the gut flora, metabolic pathways, and inflammatory pathways. It can also interfere with neurotransmitter release. There is an association between elevated levels of isovalerate and increased cortisol levels.
2-Methylbutyrate	Branched chain fatty acid.
Isocaproate	Produced primarily through the fermentation of branched chain amino acids (BCAAs), particularly leucine. Energy source for many tissues, especially during fasting or low carbohydrate intake.

SCFAs are known to have numerous health effects and can enhance fecal excretion of bile acids.

Low levels of SCFAs are linked to various conditions, including irritable bowel syndrome, obesity, and inflammatory bowel disease.



StoolOMX™

Advanced Bile Acid Testing and Short-Chain Fatty Acid Evaluation in One GI-MAP Add-on Panel

GI-MAP PATTERNS

Understanding Common Dysbiosis Patterns With GI-MAP

INSUFFICIENCY DYSBIOSIS

Insufficiency dysbiosis is characterized by low levels of beneficial bacteria that provide critical support for healthy intestinal and immune function. Insufficient levels of beneficial bacteria may result in an elevated risk of intestinal infections, increased intestinal barrier permeability, decreased protective factors such as secretory IgA, and increased inflammation. Lack of keystone bacteria is common in autoimmune, allergic, and chronic inflammatory conditions.

Table 18.

Markers Characterizing Insufficiency Dysbiosis	
Commensal/Keystone Bacteria: *(low levels)*	*Bacteroides fragilis* *Bifidobacterium* spp. *Enterococcus* spp. *Escherichia* spp. *Lactobacillus* spp. *Akkermansia muciniphilia* *Faecalbacterium prausnitzii* *Roseburia* spp.
Phyla Microbiota: *(low levels)*	*Bacteroidetes* *Firmicutes*
Associated Intestinal Health Markers:	Secretory IgA *(often low to very low levels)* Zonulin *(sometimes elevated)*

INFLAMMATORY DYSBIOSIS

Inflammatory dysbiosis is characterized by moderate to high levels of certain pathogens, normal microbiota, and opportunistic microbes that promote inflammation and increased intestinal permeability. Many pro-inflammatory microbes are gram-negative bacteria that belong to the Proteobacteria phylum and produce a form of lipopolysaccharide *(LPS)* that is a potent activator of inflammatory responses. This pattern is common in chronic immune and inflammatory conditions.

Table 19.

Markers Characterizing Inflammatory Dysbiosis	
Pathogens *(low to high levels)*	*Campylobacter* *C. difficile* *Pathogenic E. coli* *Salmonella* *Vibrio cholerae* *Yersinia enterocolitica* *Giardia*
Commensal/Keystone Bacteria *(high levels)*	*Escherichia* spp. *Enterobacter* spp.
Opportunistic Bacteria, Yeast, and Protozoa *(moderate to high levels)*	*Morganella* spp. *Pseudomonas* spp. *Pseudomonas aeroginosa* *Desulfovibrio* spp. *Citrobacter* spp. *Citrobacter freundii* *Klebsiella* spp. *Klebsiella pneumoniae* *Proteus* spp. *Proteus mirabilis* *Fusobacterium* spp. *Candida* spp. *Candida albicans* *Parasitic protozoa (specifically Giardia and Blastocystis hominis)*
Associated Intestinal Health Markers:	β-Glucuronidase *(may be elevated)* Occult Blood-FIT *(may be elevated)* Secretory IgA *(often low levels, but sometimes elevated)* Calprotectin *(often elevated, but sometimes very low levels)* Eosinophil Activation Protein (EDN/EPX) *(may be elevated)* Zonulin *(may be elevated in some cases)*

DIGESTIVE DYSFUNCTION DYSBIOSIS

Dysbiosis associated with digestive dysfunction is very common, and is often due to low stomach acid (hypochlorhydria), insufficient bile acids, poor digestion *(pancreatic insufficiency or brush border enzyme deficiency),* reduced absorption, and altered gastrointestinal motility. Altered digestion and motility can result in imbalances in the microbiome, characterized by overgrowth of certain species. Symptoms associated with digestive dysfunction include but are not limited to: excessive gas and bloating, abdominal discomfort, dyspepsia, heart burn, gastroesophageal reflux (GERD), constipation or diarrhea, food sensitivities and intolerances.

Table 20.

Markers Associated with Digestive Dysfunction	
Pathogens *(low to high levels)*	Most types, especially if multiple pathogens are present
H. pylori *(moderate to high levels)*	*Helicobacter pylori* *(with or without virulence factors)*
Commensal/Keystone Bacteria *(high levels)*	*Enterococcus* *Lactobacillus*
Phyla Microbiota *(high levels)*	*Bacteroidetes* and/or *Firmicutes*
Opportunistic Bacteria, Yeast, and Protozoa *(moderate to high levels)*	*Bacillus* spp. *Enterococcus faecalis* *Enterococcus faecium* *Morganella* spp. *Staphylococcus* spp. *Staphylococcus aureus* *Streptococcus* spp. *Methanobacteriaceae (family)* *Desulfovibrio* spp. *Klebsiella pneumoniae* *Prevotella* *Candida* spp. *Candida albicans* *Parasitic protozoa*
Intestinal Health Markers:	Elastase-1 *(often low to moderately low levels)* Steatocrit *(sometimes elevated)*

PATTERNS ASSOCIATED WITH IMMUNE-MEDIATED FOOD REACTIONS

The GI-MAP® (Microbial Assay Plus) can be used in conjunction with IgG Food Explorer™ and IgE Allergy Explorer™ to dig deeper into the root cause of adverse food reactions. If the gut barrier is permeable and/or digestion is suboptimal, maldigested food proteins can trigger immune system responses.

These are the key patterns to look for on the GI-MAP that are connected food sensitivities and allergies.

Table 21.

Food Intolerance, Allergy, and Adverse Food Reactions Pattern			
Histamine Producing Bacteria	*Morganella* spp.	High	*Opportunists (page 3)*
	Pseudomonas spp.		
	Pseudomonas aeroginosa		
	Citrobacter freundii		
	Klebsiella spp.		
	Klebsiella pneumoniae		
	Proteus spp.		
	Proteus mirabilis		
	Enterobacter spp.		
	Escherichia spp.		
	Fusobacterium spp.		
Mast Cell-Activating Bacteria	*H. pylori*	High	*H. pylori Panel (page 2)*
	Enterococcus faecalis	High	*Opportunists (page 3)*
	Pseudomonas aeruginosa		
	Staphylococcus aureus		
	Streptococcus spp.		
	Candida spp.	High	*Fungi/Yeast (page 3)*
	Candida albicans		
	Lipopolysaccharide producers	High	*Throughout report*
Commensal/Keystone Bacteria	*Lactobacillus* spp.	Low	*Commensal/Keystone Bacteria (page 2)*
Intestinal Health Markers	*Eosinophil Activation Protein* (EDN/EPX)	High	*Intestinal Health Markers (page 4)*
	SIgA		
	Anti-gliadin IgA		
	Zonulin		

Continued...

Table 21a.

Gut Barrier Permeability ("Leaky Gut") Pattern			
Intestinal Permeability	Any Pathogen	High	*Pathogens (page 1)*
	Lactobacillus spp.	Low	*Commensal/Keystone Bacteria (page 2)*
	Akkermansia muciniphila	Low; <dl	
	Candida albicans	High	*Fungi/Yeast (page 3)*
	Anti-gliadin IgA	High	*Intestinal Health Markers (page 4)*
	Zonulin		
Low Butyrate/SCFA Production	*Faecalibacterium prausnitzii*	Low; <dl	*Commensal/Keystone Bacteria (page 2)*
	Roseburia spp.	Low	
	Firmicutes phylum		
Poor Mucosal Health	*Bifidobacterium* spp.	Low; <dl	*Commensal/Keystone Bacteria (page 2)*
	Escherichia spp.	Low	
	Lactobacillus spp.		
	Akkermansia muciniphila	Low; dl	
	Bacteroidetes phylum	Low	

Table 21b.

Digestive Insufficiency Pattern			
Digestive Insufficiency	*Firmicutes phylum*	High	*Commensal/Keystone Bacteria (page 2)*
	Bacteroidetes phylum		
	Enterococcus spp.		
	Lactobacillus spp.		
	Akkermansia muciniphila		
	Bacillus spp.	High	*Opportunists (page 3)*
	Enterococcus faecalis		
	Enterococcus faecium		
	Staphylococcus spp.		
	Staphylococcus aureus		
	Streptococcus spp.		
	Desulfovibrio spp.		
	Methanobacteriaceae (family)		
	Fusobacterium spp.		
	Steatocrit	Detected; High	*Intestinal Health Markers (page 4)*
	Pancreatic Elastase-1	Low	

GAS & HISTAMINE PRODUCERS ON GI-MAP

Table 22.

Primary Hydrogen Producers	*Faecalibacterium prausnitzii*
	Roseburia spp.
	Bacteroidetes phyla
	Firmicutes phyla
Primary Methane Producers	*Methanobacteriaceae (family)*
Primary Hydrogen Sulfide Producers	*Bacteroides fragilis*
	Escherichia spp.
	Enterobacter spp.
	Desulfovibrio spp.
	Morganella spp.
	Pseudomonas aeruginosa
	Staphylococcus aureus
	Citrobacter spp.
	Citrobacter freundii
	Klebsiella spp.
	Klebsiella pneumoniae
	Proteus spp.
	Proteus mirabilis
	Fusobacterium spp.
Histamine Producing Bacteria	*Lactobacillus* spp.
	Morganella spp.
	Pseudomonas
	Pseudomonas aeruginosa
	Citrobacter freundii
	Klebsiella
	Klebsiella pneumoniae
	Proteus
	Proteus mirabilis
	Enterobacter spp.
	Escherichia spp.
	Fusobacterium spp.

MICROBE CATEGORIES

Table 23.

Primary Hydrogen Producers
Faecalibacterium prausnitzii
Roseburia spp.
Bacteroidetes phyla
Firmicutes phyla

Primary Methane Producers
Methanobacteriaceae (family)

Primary Hydrogen Sulfide Producers
Bacteroides fragilis
Escherichia spp.
Enterobacter spp.
Desulfovibrio spp.
Morganella spp.
Pseudomonas aeruginosa
Staphylococcus aureus
Citrobacter spp.
Citrobacter freundii
Klebsiella spp.
Klebsiella pneumoniae
Proteus spp.
Proteus mirabilis
Fusobacterium spp.

Histamine Producing Bacteria
Lactobacillus spp.
Morganella spp.
Pseudomonas
Pseudomonas aeruginosa
Citrobacter freundii
Klebsiella
Klebsiella pneumoniae
Proteus
Proteus mirabilis
Enterobacter spp.
Escherichia spp.
Fusobacterium spp.

Mast Cell-Activating Microbes
H. pylori
Enterococcus faecalis
Pseudomonas aeruginosa
Staphylococcus aureus
Streptococcus spp.
Candida spp.
Candida albicans
Lipopolysaccharide producers *(see LPS list)*

Lipopolysaccharide (LPS) Producing Bacteria
Escherichia spp.
Enterobacter spp.
Morganella spp.
Pseudomonas spp.
Pseudomonas aeruginosa
Citrobacter spp.
Citrobacter freundii
Klebsiella spp.
Klebsiella pneumoniae
Proteus
Proteus mirabilis

SUPPORT INFO

877-485-5336

METHODOLOGY

Quantitative PCR (qPCR) or Real-Time Polymerase Chain Reaction (RT-PCR) — *provides you with true quantitative values. It helps differentiate trace levels of an organism from frank elevations indicative of active infection.*

SPECIMEN REQUIREMENTS

Single Stool Sample — *at ambient room temperature in specimen vial provided.*

TEST ORDERING OPTIONS

- **GI-MAP® | GI Microbial Assay Plus**
- **GI-MAP® + Zonunlin**
- **GI Pathogens Profile**
- ***H. pylori* Profile**
- **Zonulin Profile** (Stool)
- **Calprotectin** (Stand-alone)
- **Gluten Peptide** (Add-on or stand-alone)
- **Universal Antibiotic Resistance Genes Panel** (Add-on only)
- **StoolOMX™** (Add-on only)

Build Your GI-MAP Knowledge With Our Complimentary Educational Services at DSL Academy:

DSL Academy (DSLA) is an exclusive, online learning platform designed to help you better interpret the GI-MAP test. The DSLA curriculum is taught by the DSL Medical Education Team and is available to all active DSL account holders. *Learn more at: www.diagnosticsolutionslab.com/clinicians/dsl-academy.*

DSL ACADEMY

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Diagnostic Solutions laboratory
Phone: 877-485-5336
Email: cs@diagnosticsolutionslab.com
Web: diagnosticsolutionslab.com

SAMPLE REPORT

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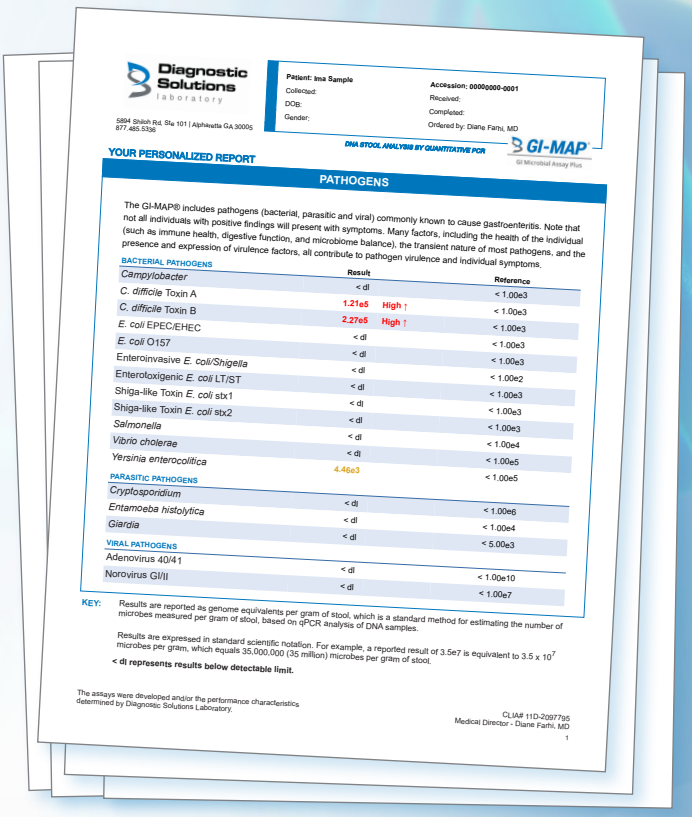

Diagnostic Solutions laboratory

5894 Shiloh Rd, Ste 101 | Alpharetta GA 30005
877.485.5336

Patient: Ima Sample
Collected:
DOB:
Gender:

Accession: 00000000-0001
Received:
Completed:
Ordered by: Diane Farhi, MD

DNA STOOL ANALYSIS BY QUANTITATIVE PCR — GI-MAP GI Microbial Assay Plus

YOUR PERSONALIZED REPORT

PATHOGENS

The GI-MAP® includes pathogens (bacterial, parasitic and viral) commonly known to cause gastroenteritis. Note that not all individuals with positive findings will present with symptoms. Many factors, including the health of the individual (such as immune health, digestive function, and microbiome balance), the transient nature of most pathogens, and the presence and expression of virulence factors, all contribute to pathogen virulence and individual symptoms.

BACTERIAL PATHOGENS	Result		Reference
Campylobacter	< dl		< 1.00e3
C. difficile Toxin A	1.21e5	High ↑	< 1.00e3
C. difficile Toxin B	2.27e5	High ↑	< 1.00e3
E. coli EPEC/EHEC	< dl		< 1.00e3
E. coli O157	< dl		< 1.00e3
Enteroinvasive *E. coli*/*Shigella*	< dl		< 1.00e2
Enterotoxigenic *E. coli* LT/ST	< dl		< 1.00e3
Shiga-like Toxin *E. coli* stx1	< dl		< 1.00e3
Shiga-like Toxin *E. coli* stx2	< dl		< 1.00e3
Salmonella	< dl		< 1.00e4
Vibrio cholerae	< dl		< 1.00e5
Yersinia enterocolitica	4.46e3		< 1.00e5
PARASITIC PATHOGENS			
Cryptosporidium	< dl		< 1.00e6
Entamoeba histolytica	< dl		< 1.00e4
Giardia	< dl		< 5.00e3
VIRAL PATHOGENS			
Adenovirus 40/41	< dl		< 1.00e10
Norovirus GI/II	< dl		< 1.00e7

KEY: Results are reported as genome equivalents per gram of stool, which is a standard method for estimating the number of microbes measured per gram of stool, based on qPCR analysis of DNA samples.

Results are expressed in standard scientific notation. For example, a reported result of 3.5e7 is equivalent to 3.5×10^7 microbes per gram, which equals 35,000,000 (35 million) microbes per gram of stool.

< dl represents results below detectable limit.

The assays were developed and/or the performance characteristics determined by Diagnostic Solutions Laboratory.

CLIA# 11D-2097795
Medical Director - Diane Farhi, MD

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INTERPRETIVE GUIDE

GI-MAP® – Unparalleled DNA Based Stool Testing

Our mission: to deliver innovative, accurate and clinically relevant diagnostic testing in a timely and cost-effective manner

GI-MAP®
GI Microbial Assay Plus