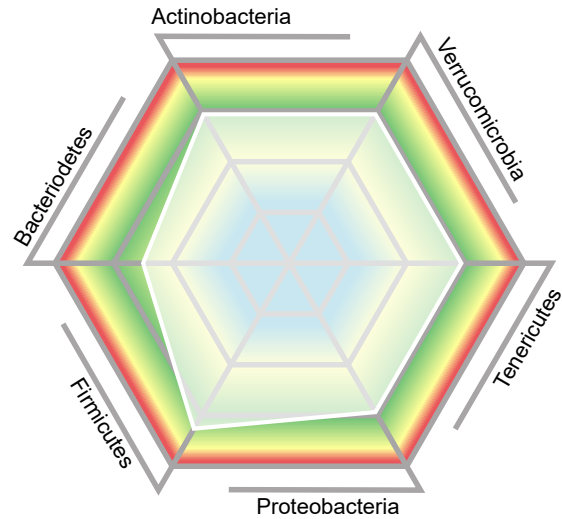
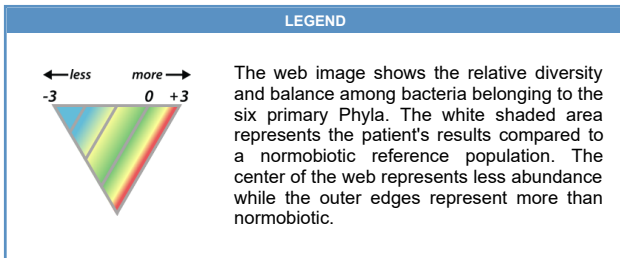


TEST NAME: GI360 Microbiome x1

GI360™; stool

Microbiome Abundance and Diversity Summary

The abundance and diversity of gastrointestinal bacteria provide an indication of gastrointestinal health, and gut microbial imbalances can contribute to dysbiosis and other chronic disease states. The GI360™ Microbiome Profile is a gut microbiota DNA analysis tool that identifies and characterizes more than 45 targeted analytes across six Phyla using PCR and compares the patient results to a characterized normobiotic reference population. The web chart illustrates the degree to which an individual's microbiome profile deviates from normobiosis.



Dysbiosis Index

The Dysbiosis Index (DI) is calculated strictly from the results of the Microbiome Profile, with scores from 1 to 5. A DI score above 2 indicates dysbiosis; a microbiota profile that differs from the defined normobiotic reference population. The higher the DI above 2, the more the sample deviates from the normobiotic profile. The dysbiosis test and DI does not include consideration of dysbiotic and pathogenic bacteria, yeast, parasites and viruses that may be reported in subsequent sections of the GI360™ test.

DI Score

2



GI 360 Key Findings

Phascolarctobacterium spp., Very High ↑

TEST NAME: GI360 Microbiome x1

Microbiome Bacterial Abundance; Multiplex PCR

LEGEND						
-3	-2	-1	0	+1	+2	+3
Very Low		Low	Within Reference Interval	High		Very High

Results are graphed as deviations from a normobiotic population. Normobiosis or a normobiotic state characterizes a composition of the microbiota profile in which microorganisms with potential health benefits predominate in abundance and diversity over potentially harmful ones.

Actinobacteria	Result	-3	-2	-1	0	+1	+2	+3	Reference Interval
Actinobacteria	0				▲				0
Actinomycetales	0				▲				0
Bifidobacterium spp.	0				▲				0
Bacteroidetes	Result	-3	-2	-1	0	+1	+2	+3	Reference Interval
Alistipes spp.	0				▲				0
Alistipes onderdonkii	0				▲				0
Bacteroides fragilis	0				▲				0
Bacteroides spp. & Prevotella spp.	0				▲				0
Bacteroides spp.	-1			▲					0
Bacteroides pectinophilus	0				▲				0
Bacteroides stercoris	0				▲				0
Bacteroides zooglyphiformans	0				▲				0
Parabacteroides johnsonii	0				▲				0
Parabacteroides spp.	0				▲				0
Firmicutes	Result	-3	-2	-1	0	+1	+2	+3	Reference Interval
Firmicutes	0				▲				0
Bacilli Class	0				▲				0
Catenibacterium mitsuokai	0				▲				0

Notes:

The gray-shaded area of the bar graph represents reference values outside the reporting limits for this test.

*This test was developed and its performance characteristics determined by Doctor's Data Laboratories in a manner consistent with CLIA requirements. The U. S. Food and Drug Administration (FDA) has not approved or cleared this test; however, FDA clearance is not currently required for clinical use. The results are not intended to be used as a sole means for clinical diagnosis or patient management decisions.

Methodology: Multiplex PCR

TEST NAME: GI360 Microbiome x1

Microbiome Bacterial Abundance; Multiplex PCR

Firmicutes	Result	-3	-2	-1	0	+1	+2	+3	Reference Interval
Clostridia Class	0				▲				0
<i>Clostridium methylpentosum</i>	-1			▲					0
<i>Clostridium</i> L2-50	0				▲				0
<i>Coprobacillus cateniformis</i>	0				▲				0
<i>Dialister invisus</i>	0				▲				0
<i>Dialister invisus</i> & <i>Megasphaera micronuciformis</i>	0				▲				0
<i>Dorea</i> spp.	-1			▲					0
<i>Eubacterium bifforme</i>	0				▲				0
<i>Eubacterium hallii</i>	-1			▲					0
<i>Eubacterium rectale</i>	-1			▲					0
<i>Eubacterium siraeum</i>	0				▲				0
<i>Faecalibacterium prausnitzii</i>	0				▲				0
Lachnospiraceae	0				▲				0
<i>Lactobacillus ruminis</i> & <i>Pediococcus acidilactici</i>	0				▲				0
<i>Lactobacillus</i> spp.	0				▲				0
<i>Phascolarctobacterium</i> spp.	+2						▲		0
<i>Ruminococcus albus</i> & <i>R. bromii</i>	0				▲				0
<i>Ruminococcus gnavus</i>	0				▲				0
<i>Streptococcus agalactiae</i> & <i>Eubacterium rectale</i>	0				▲				0
<i>Streptococcus salivarius</i> ssp. <i>thermophilus</i> & <i>S. sanguinis</i>	0				▲				0

Notes:

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Methodology: Multiplex PCR

TEST NAME: GI360 Microbiome x1

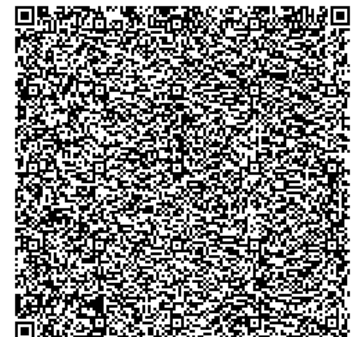
Microbiome Bacterial Abundance; Multiplex PCR

Firmicutes	Result	-3	-2	-1	0	+1	+2	+3	Reference Interval
<i>Streptococcus salivarius</i> ssp. <i>thermophilus</i>	-1			▲					0
<i>Streptococcus</i> spp.	0				▲				0
<i>Veillonella</i> spp.	0				▲				0
Proteobacteria	Result	-3	-2	-1	0	+1	+2	+3	Reference Interval
Proteobacteria	0				▲				0
<i>Enterobacteriaceae</i>	0				▲				0
<i>Escherichia</i> spp.	0				▲				0
<i>Acinetobacter junii</i>	0				▲				0
Tenericutes	Result	-3	-2	-1	0	+1	+2	+3	Reference Interval
<i>Mycoplasma hominis</i>	0				▲				0
Verrucomicrobia	Result	-3	-2	-1	0	+1	+2	+3	Reference Interval
<i>Akkermansia muciniphila</i>	0				▲				0



Microbiome Abundance Information:

- The GI360™ Microbiome Profile is a focused gut microbiota DNA analysis tool that identifies more than 45 targeted analytes across six phyla using a CE-marked multiplex PCR system. Patient results are compared to a highly defined normobiotic reference population (n > 1,100). The white shadowed web plot within the hexagonal diagram illustrates the degree to which an individual's microbiome profile deviates from normobiosis. The center of the diagram represents less bacterial abundance while the outer edges represent greater than normobiosis. Deviation from a hexagon-shaped plot indicates variant diversity of the microbial community. Key findings for patient's microbiome profile are summarized in the table below the diagram, and detailed results for all of the analytes are presented on the next 3 pages of the report. Detailed results for the specific bacteria are reported as -3 to +3 standard deviations, as compared to the normobiotic reference population.



Notes:

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Methodology: Multiplex PCR

TEST NAME: GI360 Microbiome x1

Commentary

Introduction

This analysis of the stool specimen provides fundamental information about the overall gastrointestinal health of the patient. When abnormal microflora or significant aberrations in intestinal health markers are detected, specific commentaries are presented. If no significant abnormalities are found, commentaries are not presented.

Microbiome Abundance Information

Actinobacteria (phylum)

Actinobacteria is one of the largest bacterial phyla, comprised of Gram-positive bacteria. This phylum includes a wide range of species, with different morphological and physiological characteristics. Significant groups in the human colon include Actinomycetales and Bifidobacteriales. Actinomycetales were inversely associated with clinically significant depression in IBS patients, suggesting these bacteria may be depleted in depressed IBS patients. A strict vegetarian diet may increase the total count of *Actinomyces* spp. compared to following a Western diet.

Bacteroidetes (phylum)

Bacteroidetes make up approximately 28% of the gut microbiota in healthy human adults. They are early colonizers of the infant gut and are amongst the most stable, at a species and strain level, in the host. A low preponderance of Bacteroidetes in relation to Firmicutes has been associated with obesity, though this can increase with weight loss and restricted calorie intake.

↓ *Bacteroides* (species)

Species in the genus *Bacteroides* carry out broad metabolic functions, including degradation of complex plant polysaccharides, proteolytic activities, de-conjugation of bile acids, mucosal barrier integrity, short chain fatty acid production, fatty acid storage and glucose metabolism. *Bacteroides* spp. are maintained at a higher abundance in breastfed individuals into adulthood. *Bacteroides fragilis* plays an important role in the prevention of intestinal inflammation. An energy-restricted diet has been shown to increase *B. fragilis* in overweight adolescents. An increase in *B. stercoris* has been associated with higher risk of colon cancer. Decreased levels of *Bacteroides* spp. have been reported in association with multiple sclerosis, rheumatoid arthritis and Parkinson's disease.

Firmicutes (phylum)

The phylum Firmicutes constitutes the most diverse and abundant group of gastrointestinal microbiota which are grouped into four classes, Bacilli, Clostridia, Erysipelotrichia, and Negativicutes. They constitute about 39% of gut bacteria in healthy adults, but may increase to as high as 80% in an imbalanced microbial community.

↓ *Clostridium methylpentosum* (species)

Appropriate digestion and metabolism of complex dietary carbohydrates from plants drives healthy diversity in the gut microbiota. *Clostridium methylpentosum* ferments the naturally occurring sugar L-rhamnose that is released by microbial breakdown of plant-derived pectin. Rhamnose is fermented to propionate and acetate which are short chain fatty acids that have pivotal regulatory roles in the maintenance of mucosal barrier integrity, gut microbiota balance, post-prandial appetite suppression and normoglycemia. Lower levels of *C. methylpentosum* were reported for children with autism and pervasive developmental disorder compared to neurotypicals controls. Consumption of probiotic yogurt LKM512 containing *Bifidobacterium animalis* (subspecies lactis LKM512) increased the levels of *C. methylpentosum*.

↓ *Dorea* (genus)

Dorea is a genus within the *Lachnospiraceae* family that is in the Firmicutes phylum. *Dorea* species are known to produce hydrogen and carbon dioxide as end-products of glucose fermentation and may be associated with bloating. Decreased levels of *Dorea* spp. were observed in patients with Parkinson's disease. Recent studies have identified increased levels of *Dorea* spp. in patients diagnosed with IBS, nonalcoholic fatty liver disease and non-alcoholic steatohepatitis, multiple sclerosis and colorectal cancer.

↓ *Eubacterium hallii* (species)

Eubacterium hallii and *Eubacterium rectale* are both part of the *Lachnospiraceae* family that is in the Firmicutes phylum. *E. hallii* and *E. rectale* produce butyrate that is a key regulator of mucosal barrier integrity and function. Decreased levels of *Eubacterium* spp. have been associated with very high protein diets. *Eubacterium hallii* is capable of metabolizing glucose into products with antimicrobial properties.

TEST NAME: GI360 Microbiome x1

Commentary

Microbiome Abundance Information continued...

↓ ***Eubacterium rectale* (species)**

Eubacterium rectale is part of the *Lachnospiraceae* family and produces butyrate. *Eubacterium rectale* was found to be in lower abundance in patients with type 2 diabetes, colorectal cancer, and chronic idiopathic diarrhea. There is a negative correlation between *Eubacterium rectale* levels and the symptomatology of irritable bowel syndrome (IBS). Decreased levels of *Eubacterium* spp. have been associated with very high protein diets.

↑ ***Phascolarctobacterium* (genus)**

Phascolarctobacterium are in the Firmicutes phylum. *Phascolarctobacterium* can produce short chain fatty acids, including acetate and propionate, and may be associated with metabolic effects and mental state of the host. Patients diagnosed with major depressive disorder had increased levels of these species. Decreased levels of *Phascolarctobacterium* were found to be associated with Crohn's disease, ulcerative colitis and Alzheimer's disease. Consumption of cruciferous vegetables, such as broccoli, increases the abundance of *Phascolarctobacterium* in the gut.

↓ ***Streptococcus* (genus)**

Higher abundance of *S. salivarius* and *S. thermophilus* (Firmicutes phylum) have been associated with a moderate to severe disease course in newly diagnosed ulcerative colitis (UC) patients. These findings are in accordance with a study that showed that UC patients have significantly increased *Streptococcus* spp. and depletion of *Bifidobacterium* spp. Higher levels of *Streptococcus* spp. were also observed in patients with colorectal cancer compared to healthy controls. Administration of *S. salivarius* together with *Bifidobacterium bifidum* was shown to reduce the incidence of acute diarrhea and rotavirus shedding in infants. *S. salivarius* and *S. thermophilus* are also widely used in dairy products like yogurt and cheese.

Proteobacteria (phylum)

Proteobacteria include a wide variety of pathogens, including species within the *Escherichia*, *Shigella*, *Salmonella*, *Vibrio*, and *Helicobacter* genera. The phylum includes a number of species that are permanent residents of the microbiota and capable of inducing nonspecific inflammation and diarrhea when their presence is increased. Proteobacteria make up approximately 2% of the gut microbiota in healthy adults.

Tenericutes (phylum)

Tenericutes are cell wall-less bacteria that do not synthesize precursors of peptidoglycan. Tenericutes consist of four main clades designated as the *Acholeplasma*, *Spiroplasma*, *Pneumoniae* and *Hominis* clusters. Tenericutes are typically parasites or commensals of eukaryotic hosts.

Verrucomicrobia (phylum)

Verrucomicrobia is a less common phylum in the human gut microbiota, but one with increasing recognition with regards to health. Verrucomicrobia includes *Akkermansia muciniphila*. The obligate anaerobe *A. muciniphila* constitutes 3-5% of total bacteria in a healthy microbiome, and has a protective or anti-inflammatory role in the intestinal mucosa.