DRAFT

GENOVA DIAGNOSTICS

3425 Corporate Way
Duluth, GA 30096

GI fx GI Effects Stool Profiles

Patient:

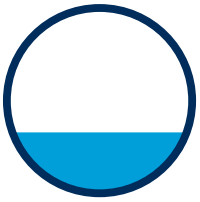
DOB:
Sex:
MRN:

2200 GI Effects® Comprehensive Profile - Stool

Interpretation At-a-Glance

INFECTION

INFLAMMATION



INSUFFICIENCY

Pancreatic Elastase 1 ▼

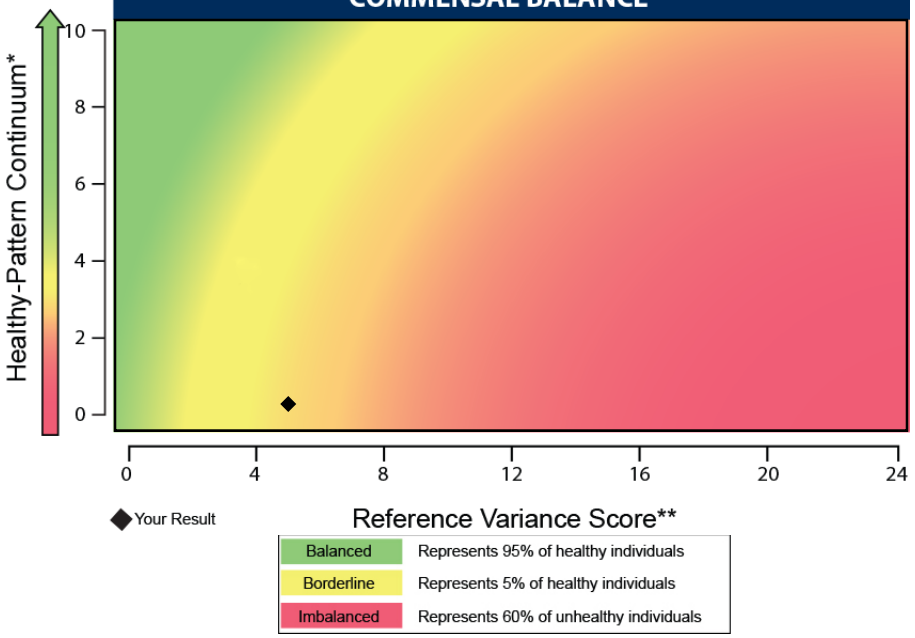
IMBALANCE

Beneficial Bacteria ▼

PP Bacteria ▲

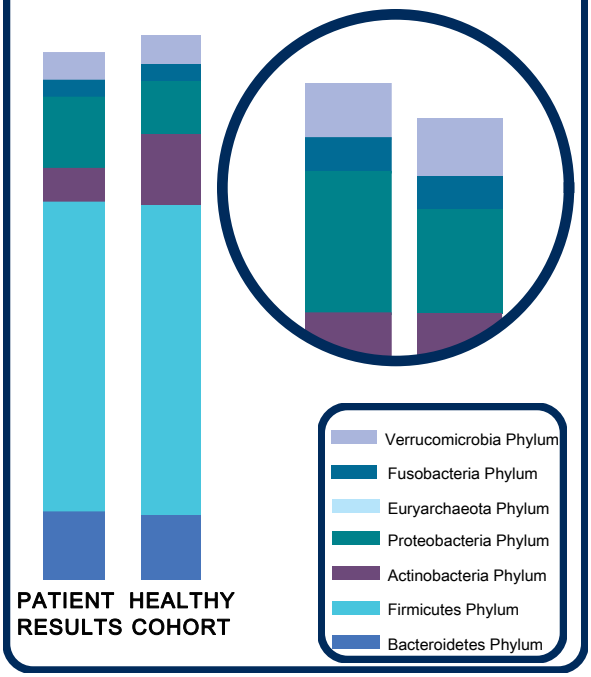
PP Yeast/Fungi ▲

COMMENSAL BALANCE



*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.
**The total number of Commensal Bacteria (PCR) that are out of reference ranges for this individual.

RELATIVE ABUNDANCE



GI Effects® Comprehensive Profile - Stool

Methodology: GC/MS, Automated Chemistry, EIA

	Results	QUINTILE DISTRIBUTION (1st 2nd 3rd 4th 5th)	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 †	158 L	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	2.6		1.8-9.9 micromol/g
Fecal Fat (Total*)	19.5		3.2-38.6 mg/g
Triglycerides	1.1		0.3-2.8 mg/g
Long-Chain Fatty Acids	12.9		1.2-29.1 mg/g
Cholesterol	0.5		0.4-4.8 mg/g
Phospholipids	5.0		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin †	<16	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	0.6	1.1 4.6	<=4.6 mcg/g
Fecal secretory IgA	206		<=885 mcg/g
Gastrointestinal Microbiome			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	47.5		>=23.3 micromol/g
n-Butyrate Concentration	10.6		>=3.6 micromol/g
n-Butyrate %	22.3		11.8-33.3 %
Acetate %	62.8		48.1-69.2 %
Propionate %	14.7		<=29.3 %
Beta-glucuronidase	2,297		368-6,266 U/g

**Total value is equal to the sum of all measurable parts.*

†These results are not represented by quintile values.

A. L. Peace-Brewer, PhD, D(ABMLI), Lab Director · CLIA Lic. #34D0655571 · Medicare Lic. #34-8475

Tests were developed and their performance characteristics determined by Genova Diagnostics. Unless otherwise noted with ◆, the assays have not been cleared by the U.S. Food and Drug Administration.

Methodology: DNA by PCR

Gastrointestinal Microbiome

Commensal Bacteria (PCR)	Result CFU/g stool		QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Reference Range CFU/g stool
Bacteroidetes Phylum				
Bacteroides-Prevotella group	6.1**E8**			3.4**E6**-1.5**E9**
Bacteroides vulgatus	2.6**E9**	H		<=2.2**E9**
Barnesiella spp.	<DL			<=1.6**E8**
Odoribacter spp.	8.2**E7**	H		<=8.0**E7**
Prevotella spp.	<DL	L		1.4**E5**-1.6**E7**
Firmicutes Phylum				
Anaerotruncus colihominis	4.7**E6**			<=3.2**E7**
Butyrivibrio crossotus	7.2**E4**			5.5**E3**-5.9**E5**
Clostridium spp.	1.8**E9**			1.7**E8**-1.5**E10**
Coprococcus eutactus	7.0**E5**			<=1.2**E8**
Faecalibacterium prausnitzii	2.5**E9**			5.8**E7**-4.7**E9**
Lactobacillus spp.	1.4**E8**			8.3**E6**-5.2**E9**
Pseudoflavonifractor spp.	1.9**E8**	H		4.2**E5**-1.3**E8**
Roseburia spp.	2.0**E9**			1.3**E8**-1.2**E10**
Ruminococcus spp.	3.0**E8**			9.5**E7**-1.6**E9**
Veillonella spp.	1.5**E7**			1.2**E5**-5.5**E7**
Actinobacteria Phylum				
Bifidobacterium spp.	2.8**E8**			<=6.4**E9**
Bifidobacterium longum	3.1**E7**			<=7.2**E8**
Collinsella aerofaciens	<DL	L		1.4**E7**-1.9**E9**
Proteobacteria Phylum				
Desulfovibrio piger	6.6**E4**			<=1.8**E7**
Escherichia coli	5.2**E6**			9.0**E4**-4.6**E7**
Oxalobacter formigenes	1.8**E6**			<=1.5**E7**
Euryarchaeota Phylum				
Methanobrevibacter smithii	<DL			<=8.6**E7**
Fusobacteria Phylum				
Fusobacterium spp.	1.7**E4**			<=2.4**E5**
Verrucomicrobia Phylum				
Akkermansia muciniphila	7.8**E6**			>=1.2**E6**
Firmicutes/Bacteroidetes Ratio				
Firmicutes/Bacteroidetes (F/B Ratio)	10	L		12-620

The gray-shaded portion of a quintile reporting bar represents the proportion of the reference population with results below detection limit.

Commensal results and reference range values are displayed in a computer version of scientific notation, where the capital letter “E” indicates the exponent value (e.g., 7.3E6 equates to 7.3 x 10^6 or 7,300,000).

The Firmicutes/Bacteroidetes ratio (F/B Ratio) is estimated by utilizing the lowest and highest values of the reference range for individual organisms when patient results are reported as <DL or >UL.

Methodology: culture/MALDI-TOF MS, Automated and Manual Biochemical Methods, Vitek 2® System Microbial identification and Antibiotic susceptibility

Gastrointestinal Microbiome

Human microflora is influenced by environmental factors and the competitive ecosystem of the organisms in the GI tract. Pathogenic significance should be based upon clinical symptoms.

Microbiology Legend

NG	NP	PP	P
No Growth	Non-Pathogen	Potential Pathogen	Pathogen

Additional bacteria

Non-pathogen: Organisms that fall under this category are those that constitute normal, commensal flora, or have not been recognized as etiological agents of disease.

Potential Pathogen: Organisms that fall under this category are considered potential or opportunistic pathogens when present in heavy growth.

Pathogen: The organisms that fall under this category are well-recognized pathogens in clinical literature that have a clearly recognized mechanism of pathogenicity and are considered significant regardless of the quantity that appears in culture.

Bacteriology (Culture)

			1+	2+	3+	4+
Lactobacillus spp.		NG				
Escherichia coli	4+	NP				◆
Bifidobacterium spp.	2+	NP		◆		

Additional Bacteria

			1+	2+	3+	4+
alpha hemolytic Streptococcus	4+	NP				◆
gamma haemolytic Streptococcus	2+	NP		◆		
Citrobacter amalonaticus	4+	PP				◆
Streptococcus agalactiae gp B	3+	NP			◆	

Mycology (Culture)

			1+	2+	3+	4+
Candida glabrata (T. glabrata)	3+	PP			◆	

KOH Preparation for Yeast

Methodology: Potassium Hydroxide (KOH) Preparation for Yeast

Potassium Hydroxide (KOH) Preparation for Yeast
These yeast usually represent the organisms isolated by culture. In the presence of a negative yeast culture, microscopic yeast may reflect organisms not viable enough to grow in culture. The presence of yeast on KOH prep should be correlated with the patient's symptoms. However, moderate to many yeast suggests yeast overgrowth.

	Results	The result is reported as the amount of yeast detected microscopically:
KOH Preparation, stool	Rare Yeast Detected	Rare: 1-2 per slide
		Few: 2-5 per high power field (HPF)
		Moderate: 5-10 per HPF
		Many: >10 per HPF

Parasitology

Microscopic O&P Results

Microscopic O&P is capable of detecting all described gastrointestinal parasites. The organisms listed in the box represent those commonly found in microscopic stool analysis. Should an organism be detected that is not included in the list below, it will be reported in the Additional Results section. For an extensive reference of all potentially detectable organisms, please visit www.gdx.net/product/gi-effects-comprehensive-stool-test

Genus/species	Results
Nematodes - roundworms	
Acylostoma duodenale (Hookworm)	Not Detected
Ascaris lumbricoides	Not Detected
Capillaria philippinensis	Not Detected
Enterobius vermicularis	Not Detected
Necator americanus (Hookworm)	Not Detected
Strongyloides stercoralis	**Rare Ova Detected**
Trichuris trichiura	Not Detected
Cestodes-tapeworms	
Diphyllobothrium latum	Not Detected
Dipylidium caninum	Not Detected
Hymenolepis diminuta	Not Detected
Hymenolepis nana	Not Detected
Taenia spp.	**Rare Ova Detected**
Trematodes-flukes	
Clonorchis/Opisthorchis spp.	Not Detected
Fasciola spp./*Fasciolopsis buski* ova	Not Detected
Heterophyes/Metagonimus ova	**Moderate Ova Detected**
Paragonimus spp.	Not Detected
Schistosoma spp.	Not Detected
Protozoa	
Balantidium coli	Not Detected
Blastocystis spp.	Not Detected
Chilomastix mesnili	Not Detected
Cryptosporidium spp.	Not Detected
Cyclospora cayetanensis	Not Detected
Dientamoeba fragilis	Not Detected
Entamoeba coli	Not Detected
Entamoeba dispar	Not Detected
Entamoeba hartmanni	Not Detected
Entamoeba histolytica	Not Detected
Entamoeba polecki	Not Detected
Endolimax nana	Not Detected
Giardia	Not Detected
Iodamoeba butschlii	Not Detected
Isospora spp.	Not Detected
Trichomonads (e.g. *Pentatrichomonas*)	Not Detected
Additional Findings	
Charcot-Leyden Crystals	Not Detected
Meat Fibers	Not Detected
Vegetable Fibers	Not Detected
White Blood Cells	Not Detected
Other Infectious Findings	Additional Organism, Additional Organism, Additional Organism

** Indicates testing performed by Genova Diagnostics, Inc. 63 Zillicoa St., Asheville, NC 28801-0174A. L. Peace-Brewer, PhD, D(ABMLI), Lab Director - CLIA Lic. #34D0655571 - Medicare Lic. #34-8475. Tests were developed and their performance characteristics determined by Genova Diagnostics.

Parasitology

PCR Parasitology - Protozoa

Organism	Results		Expected Result
Blastocystis spp.	4.00e4	**Detected**	Not Detected
Cryptosporidium spp.	<2.00e3	Not Detected	Not Detected
Cyclospora cayetanensis	<2.00e3	Not Detected	Not Detected
Dientamoeba fragilis	<2.00e3	Not Detected	Not Detected
Entamoeba histolytica	<2.00e3	Not Detected	Not Detected
Giardia	<2.00e3	Not Detected	Not Detected

Blastocystis spp. Reflex Subtyping

Type 1:	Not Detected	Type 4:	Not Detected	Type 7:	Not Detected
Type 2:	**Detected**	Type 5:	Not Detected	Type 8:	Not Detected
Type 3:	Not Detected	Type 6:	**Detected**	Type 9:	Not Detected

Additional Results

Methodology: EIA, Fecal Immunochemical Testing (FIT)

	Results	Expected Value
Fecal Occult Blood ◆	Negative	Negative
Color	Brown	
Consistency††	Formed/Normal	

Macroscopic Examination for Worms

Methodology: Macroscopic Evaluation

No larvae detected macroscopically

Zonulin Family Peptide

Methodology: EIA

	Results		Reference Range
Zonulin Family Peptide, Stool	250.0	H	22.3-161.1 ng/mL

Zonulin Family Peptide
This test is for research use only. Genova will not provide support on interpreting the test results. This test does not detect zonulin. The Scheffler paper suggests that the IDK kit may detect a zonulin family peptide, such as properdin. Genova's unpublished data demonstrated that the current IDK kit results were associated with stool inflammation biomarkers and an inflammationassociated dysbiosis profile.[1]
The performance characteristics of Zonulin Family Pepetide have been verified by Genova Diagnostics, Inc. The assay has not been cleared by U.S. Food and Drug Administration .

Reference :
1.Scheffler L, et al. Widely Used Commercial ELISA Does Not Detect Precursor of Haptoglobin2, but Recognizes Properdin as a Potential Second Member of the Zonulin Family. *Front Endocrinol*. 2018;9:22.

Add-on Testing

Methodology

	Results	Expected Value
HpSA - H. pylori	Negative	Negative
Campylobacter spp.	Negative	Negative
Shiga toxin *E. coli* ◆**	Negative	Negative
Clostridium difficile◆**	Negative	Negative
Fecal Lactoferrin ◆**	Negative	Negative

HpSA (Helicobacter pylori stool antigen)
Helicobacter pylori is a bacterium which causes peptic ulcer disease and plays a role in the development of gastric cancer. Direct stool testing of the antigen (HpSA) is highly accurate and is appropriate for diagnosis and follow-up of infection.

Campylobacter
Campylobacter jejuni is the most frequent cause of bacterial-induced diarrhea. While transmission can occur via the fecal-oral route, infection is primarily associated with the ingestion of contaminated and poorly cooked foods of animal origin, notably, red meat and milk.

Clostridium difficile
Clostridium difficile is an anaerobic, spore-forming gram-positive bacterium. After a disturbance of the gut flora (usually with antibiotics), colonization with Clostridium difficile can take place. Clostridium difficile infection is much more common than once thought.

Shiga toxin E. coli
Shiga toxin-producing Escherichia coli (STEC) is a group of bacterial strains that have been identified as worldwide causes of serious human gastrointestinal disease. The subgroup enterohemorrhagic E. coli includes over 100 different serotypes, with 0157:H7 being the most significant, as it occurs in over 80% of all cases. Contaminated food continues to be the principal vehicle for transmission; foods associated with outbreaks include alfalfa sprouts, fresh produce, beef, and unpasteurized juices.

††Results provided from patient input

Lab Comments

Methodology: Vitek 2® System Microbial Antibiotic susceptibility, Manual Minimum Inhibition Concentration

Mycology Sensitivity

Azole Antifungals

Candida glabrata (T. glabrata)	R	I	S-DD	S	NI
Fluconazole			16		
Voriconazole					0.25

Non-absorbed Antifungals

Candida glabrata (T. glabrata)	LOW INHIBITION	HIGH INHIBITION
Nystatin		

Natural Agents

Candida glabrata (T. glabrata)	LOW INHIBITION	HIGH INHIBITION
Berberine		
Caprylic Acid		
Garlic		
Undecylenic Acid		
Plant tannins		
Uva-Ursi		

Prescriptive Agents:
The R (Resistant) category implies isolate is not inhibited by obtainable levels of pharmaceutical agent.
The I (Intermediate) category includes isolates for which the minimum inhibition concentration (MIC) values usually approach obtainable pharmaceutical agent levels and for which response rates may be lower than for susceptible isolates.
The S-DD (Susceptible-Dose Dependent) category implies clinical efficacy when higher than normal dosage of a drug can be used and maximal concentration achieved.
The S (Susceptible) column implies that isolates are inhibited by the usually achievable concentrations of the pharmaceutical agent.
NI (No Interpretive guidelines established) category is used for organisms that currently do not have established guidelines for MIC interpretation.
Refer to published pharmaceutical guidelines for appropriate dosage therapy.

Nystatin and Natural Agents:
Results for Nystatin are being reported with natural antifungals in this category in accordance with laboratory guidelines for reporting sensitivities. In this assay, inhibition is defined as the reduction level on organism growth as a direct result of inhibition by a natural substance. The level of inhibition is an indicator of how effective the substance was at limiting the growth of an organism in an in vitro environment. High inhibition indicates a greater ability by the substance to limit growth, while Low Inhibition a lesser ability to limit growth. The designated natural products should be considered investigational in nature and not be viewed as standard clinical treatment substances.

Methodology: Vitek 2® System Microbial Antibiotic susceptibility, Manual Minimum Inhibition Concentration

Bacteria Sensitivity

Prescriptive Agents

Citrobacter amalonaticus	R	I	S-DD	S	NI
Ampicillin	R				
Amox./Clavulanic Acid	R				
Cephalothin	R				
Ciprofloxacin				S	
Tetracycline				S	
Trimethoprim/Sulfa				S	

Natural Agents

Citrobacter amalonaticus	LOW INHIBITION	HIGH INHIBITION
Berberine		
Oregano		
Plant Tannins		
Uva-Ursi		

Prescriptive Agents:
The R (Resistant) category implies isolate is not inhibited by obtainable levels of pharmaceutical agent.
The I (Intermediate) category includes isolates for which the minimum inhibition concentration (MIC) values usually approach obtainable pharmaceutical agent levels and for which response rates may be lower than for susceptible isolates.
The S-DD (Susceptible-Dose Dependent) category implies clinical efficacy when higher than normal dosage of a drug can be used and maximal concentration achieved.
The S (Susceptible) column implies that isolates are inhibited by the usually achievable concentrations of the pharmaceutical agent.
NI (No Interpretive guidelines established) category is used for organisms that currently do not have established guidelines for MIC interpretation.
Refer to published pharmaceutical guidelines for appropriate dosage therapy.
Natural Agents:
In this assay, inhibition is defined as the reduction level on organism growth as a direct result of inhibition by a substance. The level of inhibition is an indicator of how effective the substance was at limiting the growth of an organism in an in vitro environment. High inhibition indicates a greater ability by the substance to limit growth, while Low Inhibition a lesser ability to limit growth. The designated natural products should be considered investigational in nature and not be viewed as standard clinical treatment substances.

2200 GI Effects™ Comprehensive Profile - Stool

Interpretation At-a-Glance

Commensal Bacteria	Patient Results Out of Reference Range	Genova Diagnostics Commensal Bacteria Clinical Associations*							
		IBS	IBD	Metabolic Syndrome	Chronic Fatigue	Auto-immune	Type 2 Diabetes	High Blood Pressure	Mood Disorders
Bacteroidetes Phylum									
Bacteroides-Prevotella group		↑	↑	↑	↑	↑	↑	↑	↑
Bacteroides vulgatus	H	↑			↑	↑		↑	↑
Barnesiella spp.									
Odoribacter spp.	H								
Prevotella spp.	L	↑		↑	↑	↑		↑	↑
Firmicutes Phylum									
Anaerotruncus colihominis		↑	↑	↑	↑	↑	↑	↑	↑
Butyrivibrio crossotus									
Clostridium spp.									
Coprococcus eutactus		↑			↑	↑		↑	↑
Faecalibacterium prausnitzii		↑				↑			↑
Lactobacillus spp.									
Pseudoflavonifractor spp.	H	↑	↑	↑	↑	↑	↑	↑	↑
Roseburia spp.			↓						
Ruminococcus spp.		**↓↑**	↓	↓	↓	**↓↑**	**↓↑**	**↓↑**	**↓↑**
Veillonella spp.		↑	↑	↑	↑	↑	↑		↑
Actinobacteria Phylum									
Bifidobacterium spp.									
Bifidobacterium longum									
Collinsella aerofaciens	L	**↓↑**	**↓↑**	↓	**↓↑**	**↓↑**	**↓↑**	**↓↑**	**↓↑**
Proteobacteria Phylum									
Desulfovibrio piger									↑
Escherichia coli		↑	↑	↑	↑	↑	↑	↑	↑
Oxalobacter formigenes		↑		↑	↑				↑
Euryarchaeota Phylum									
Methanobrevibacter smithii		↑				↑			↑
Fusobacteria Phylum									
Fusobacterium spp.		↑	↑	↑	↑	↑	↑	↑	↑
Verrucomicrobia Phylum									
Akkermansia muciniphila		↓	↓	↓	↓	↓	↓	↓	↓

***Information derived from GDX results data comparing a healthy cohort to various clinical condition cohorts. The chart above showing a comparison of patient results to clincial conditions is meant for informational purposes only; it is not diagnostic, nor does it imply that the patient has a specific clinical diagnosis or condition.**

The arrows indicate Genova's clinical condition cohort test results falling below ↓ or above ↑ the reference range that is greater than that of Genova's healthy cohort.

↑↓ Indicates Genova's clincial condition cohort test results falling below and above the reference range that are greater than that of Genova's healthy cohort.

Cells with bolded arrows indicate Genova's clinical condition cohort had more test results falling above versus below **↓↑** or more below versus above **↓↑** the reference range compared to that of Genova's healthy cohort.

2200 GI Effects™ Comprehensive Profile - Stool

Interpretation At-a-Glance

Biomarker	Patient Results Out of Reference Range	Genova Diagnostics Biomarker Clinical Associations*							
		IBS	IBD	Metabolic Syndrome	Chronic Fatigue	Auto-immune	Type 2 Diabetes	High Blood Pressure	Mood Disorders
Pancreatic Elastase	L	↓	↓	↓	↓	↓	↓	↓	↓
Products of Protein Breakdown (Total)							↑↓		
Fecal Fat (Total*)		↑		↑	↑	↑	↓↑	↑	↑
Triglycerides		↑			↑	↑	↑	↑	↑
Long-Chain Fatty Acids		↑			↑	↑	↓↑	↑	↑
Cholesterol							↓↑	↑	
Phospholipids		↑	↑	↑	↑	↑	↑	↑	↑
Calprotectin			↑					↑	
Eosinophil Protein X (EPX)			↑						
Fecal secretory IgA		↑	↑	↑	↑	↑	↑	↑	↑
Short-Chain Fatty Acids (SCFA) (Total)					↓	↓			
n-Butyrate Concentration				↓					
n-Butyrate %									
Actetate %					↑↓		↓↑		
Propionate %				↑			↑	↑	
Beta-glucuronidase						↑↓			↑↓

***Information derived from GDX results data comparing a healthy cohort to various clinical condition cohorts. The chart above showing a comparison of patient results to clincial conditions is meant for informational purposes only; it is not diagnostic, nor does it imply that the patient has a specific clinical diagnosis or condition.**

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Cells with bolded arrows indicate Genova's clinical condition cohort had more test results falling above versus below ↓↑ or more below versus above ↓↑ the reference range compared to that of Genova's healthy cohort.