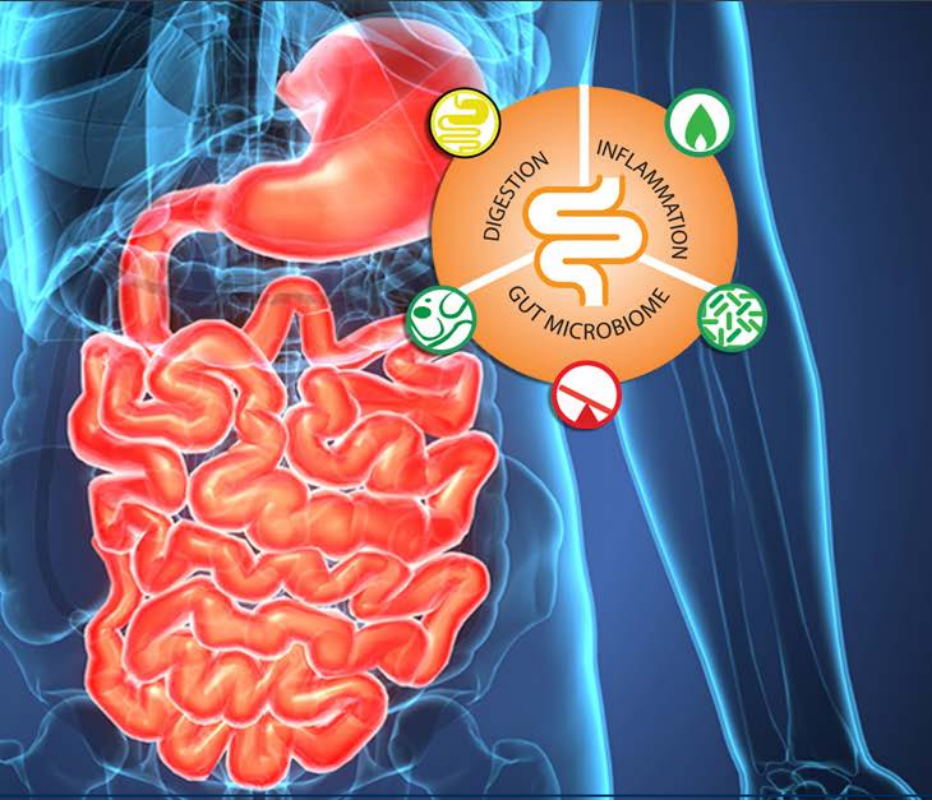
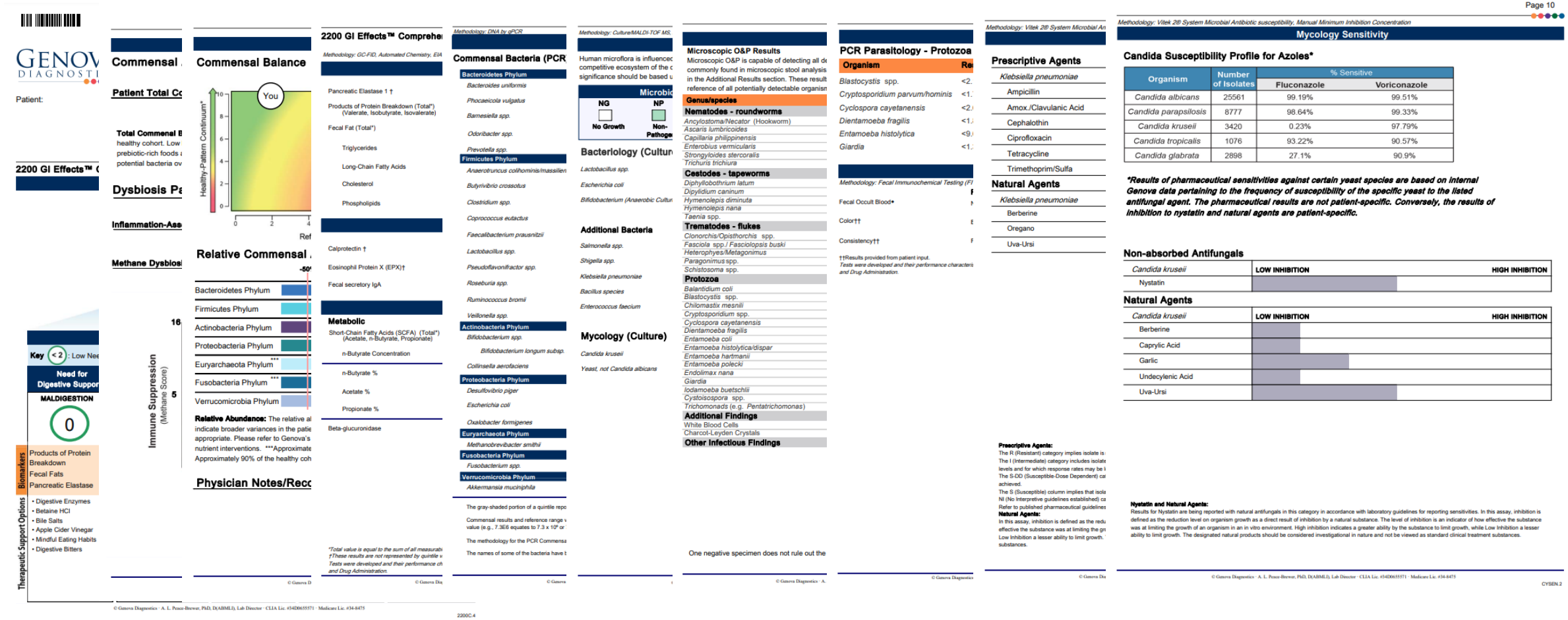


The GI Effects Comprehensive Stool Profile

Implementation: From Testing to Treatment

Patricia M. Devers, DO
Chief Clinical Officer | Genova Diagnostics

GI Effects Comprehensive Stool Profile



Patient:

2200 GI Effects™

Commensal Balance

You

Healthy-Pattern Continuum*

Relative Commensal

Bacteroidetes Phylum
Firmicutes Phylum
Actinobacteria Phylum
Proteobacteria Phylum
Euryarchaeota Phylum
Fusobacteria Phylum
Verrucomicrobia Phylum

Relative Abundance: The relative al
indicate broader variances in the patie
appropriate. Please refer to Genova's
nutrient interventions. ***Approximate
Approximately 90% of the healthy coh

Physician Notes/Recc

2200 GI Effects™ Comprehe

Methodology: GC-FID, Automated Chemistry, EIA

Pancreatic Elastase 1 †

Products of Protein Breakdown (Total*)
(Valerate, Isobutyrate, Isovalerate)

Fecal Fat (Total*)

Triglycerides

Long-Chain Fatty Acids

Cholesterol

Phospholipids

Calprotectin †

Eosinophil Protein X (EPX)†

Fecal secretory IgA

Metabolic

Short-Chain Fatty Acids (SCFA) (Total*)
(Acetate, n-Butyrate, Propionate)

n-Butyrate Concentration

n-Butyrate %

Acetate %

Propionate %

Beta-glucuronidase

*Total value is equal to the sum of all measurabl
†These results are not represented by quintile v
Tests were developed and their performance ch
and Drug Administration.

Methodology: DNA by qPCR

Commensal Bacteria (PCR

Bacteroidetes Phylum
Bacteroides uniformis
Phocaeicola vulgatus
Barnesiella spp.
Odoribacter spp.
Prevotella spp.
Firmicutes Phylum
Anaerotruncus colihominis/massilien
Butyrivibrio crossotus
Clostridium spp.
Coprococcus eutactus
Faecalibacterium prausnitzii
Lactobacillus spp.
Pseudoflavonifractor spp.
Roseburia spp.
Ruminococcus bromii
Veillonella spp.
Actinobacteria Phylum
Bifidobacterium spp.
Bifidobacterium longum subsp.
Collinsella aerofaciens
Proteobacteria Phylum
Desulfovibrio piger
Escherichia coli
Oxalobacter formigenes
Euryarchaeota Phylum
Methanobrevibacter smithii
Fusobacteria Phylum
Fusobacterium spp.
Verrucomicrobia Phylum
Akkermansia muciniphila

The gray-shaded portion of a quintile repo

Commensal results and reference range v
value (e.g., 7.3E6 equates to 7.3 x 10⁶ or

The methodology for the PCR Commensa

The names of some of the bacteria have t

Methodology: Culture/MALDI-TOF MS,

Human microflora is influence
competitive ecosystem of the
significance should be based u

Microbic

NG: No Growth
NP: Non-Pathoge

Bacteriology (Cultur

Lactobacillus spp.
Escherichia coli
Bifidobacterium (Anaerobic Cultur

Additional Bacteria

Salmonella spp.
Shigella spp.
Klebsiella pneumoniae
Bacillus species
Enterococcus faecium

Mycology (Culture)

Candida krusei
Yeast, not Candida albicans

Microscopic O&P Results

Microscopic O&P is capable of detecting all d
commonly found in microscopic stool analysis
in the Additional Results section. These result
reference of all potentially detectable organism

Genus/species

Nematodes - roundworms
Ancylostoma/Necator (Hookworm)
Ascaris lumbricoides
Capillaria philippinensis
Enterobius vermicularis
Strongyloides stercoralis
Trichuris trichiura

Cestodes - tapeworms
Diphyllobothrium latum
Dipylidium caninum
Hymenolepis diminuta
Hymenolepis nana
Taenia spp.

Trematodes - flukes
Clonorchis/Opisthorchis spp.
Fasciola spp./ Fasciolopsis buski
Heterophyes/Metagonimus
Paragonimus spp.
Schistosoma spp.

Protozoa
Balantidium coli
Blastocystis spp.
Chilomastix mesnili
Cryptosporidium spp.
Cyclospora cayetanensis
Dientamoeba fragilis
Entamoeba coli
Entamoeba histolytica/dispar
Entamoeba hartmanii
Entamoeba polecki
Endolimax nana
Giardia
Iodamoeba buetschlii
Cystoisospora spp.
Trichomonads (e.g. Pentatrichomonas)

Additional Findings
White Blood Cells
Charcot-Leyden Crystals

Other Infectious Findings

One negative specimen does not rule out the

PCR Parasitology - Protozoa

Organism	Re
Blastocystis spp.	<2.
Cryptosporidium parvum/hominis	<1.
Cyclospora cayetanensis	<2.
Dientamoeba fragilis	<1.
Entamoeba histolytica	<9.
Giardia	<1.

Methodology: Fecal Immunochemical Testing (FI

Fecal Occult Blood*
Color††
Consistency††

††Results provided from patient input.
Tests were developed and their performance characteris
and Drug Administration.

Methodology: Vitek 2® System Microbial An

Prescriptive Agents

Klebsiella pneumoniae
Ampicillin
Amox./Clavulanic Acid
Cephalothin
Ciprofloxacin
Tetracycline
Trimethoprim/Sulfa

Natural Agents

Klebsiella pneumoniae
Berberine
Oregano
Uva-Ursi

Prescriptive Agents:
The R (Resistant) category implies isolate is
The I (Intermediate) category includes isolat
levels and for which response rates may be l
The S-DD (Susceptible-Dose Dependent) ca
achieved.
The S (Susceptible) column implies that isola
NI (No Interpretive guidelines established) ca
Refer to published pharmaceutical guidelines
Natural Agents:
In this assay, inhibition is defined as the redu
effective the substance was at limiting the gr
Low Inhibition a lesser ability to limit growth.
substances.

Page 10

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

Mycology Sensitivity

Candida Susceptibility Profile for Azoles*

Organism	Number of Isolates	% Sensitive	
		Fluconazole	Voriconazole
Candida albicans	25561	99.19%	99.51%
Candida parapsilosis	8777	98.64%	99.33%
Candida kruseii	3420	0.23%	97.79%
Candida tropicalis	1076	93.22%	90.57%
Candida glabrata	2898	27.1%	90.9%

*Results of pharmaceutical sensitivities against certain yeast species are based on internal Genova data pertaining to the frequency of susceptibility of the specific yeast to the listed antifungal agent. The pharmaceutical results are not patient-specific. Conversely, the results of inhibition to nystatin and natural agents are patient-specific.

Non-absorbed Antifungals

Candida kruseii	LOW INHIBITION	HIGH INHIBITION
Nystatin		

Natural Agents

Candida kruseii	LOW INHIBITION	HIGH INHIBITION
Berberine		
Caprylic Acid		
Garlic		
Undecylenic Acid		
Uva-Ursi		

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.

Immune Suppression (Methane Score)

Key < 2 : Low Nee

Need for Digestive Suppor

MALDIGESTION

0

Biomarkers
Products of Protein Breakdown
Fecal Fats
Pancreatic Elastase

Therapeutic Support Options
- Digestive Enzymes
- Betaine HCl
- Bile Salts
- Apple Cider Vinegar
- Mindful Eating Habits
- Digestive Bitters

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2200C.4

CYSEN.2

GENOVA DIAGNOSTICS

Objectives for This Presentation

- Review case studies of various conditions
- Outline patterns for each condition seen on the GI Effects
- Discuss next steps – further testing and treatment

GENOVA DIAGNOSTICS

Case Study #1

- 41 yo female
- Standard American Diet
- Nonsmoker, no EtOH
- Only medication is OTC laxatives prn

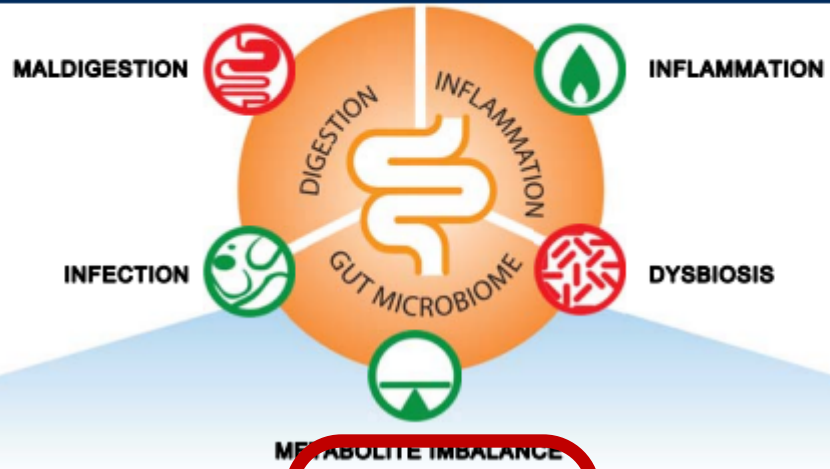
- Long history of “IBS”
- Bloating
- Alternating constipation and diarrhea
- Recent weight gain

GENOVA DIAGNOSTICS

2200 GI Effects™ Comprehensive Profile - Stool

Powered by ***Genova AI***

Results Overview



Functional Imbalance Scores

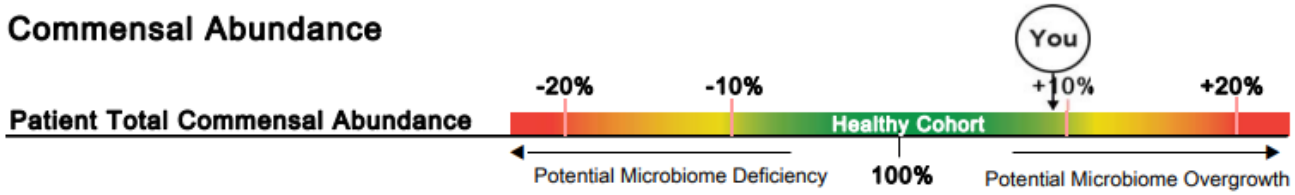
Key (< 2) : Low Need for Support (2-3) : Optional Need for Support (4-6) : Moderate Need for Support (7-10) : High Need for Support

	Need for Digestive Support	Need for Inflammation Modulation	Need for Microbiome Support	Need for Prebiotic Support	Need for Antimicrobial Support
	MALDIGESTION	INFLAMMATION	DYSBIOSIS	METABOLIC IMBALANCE	INFECTION
	10	0	9	1	0
Biomarkers	Fecal Fats ▲	Calprotectin ●	Reference Variance ▲	Beta-glucuronidase ▼	Parasitic Infection ●
	Products of Protein Breakdown △	Eosinophil Protein X ●	IAD/Methane Score △	SCFA (%) △	Pathogenic Bacteria ●
		Secretory IgA ●	PP Bacteria/Yeast ●	Total SCFA's ●	PP Bacteria/Yeast ●
	Pancreatic Elastase ▽	Occult Blood ●	Total Abundance ●	n-Butyrate Conc. ●	Total Abundance ●

GENOVA DIAGNOSTICS

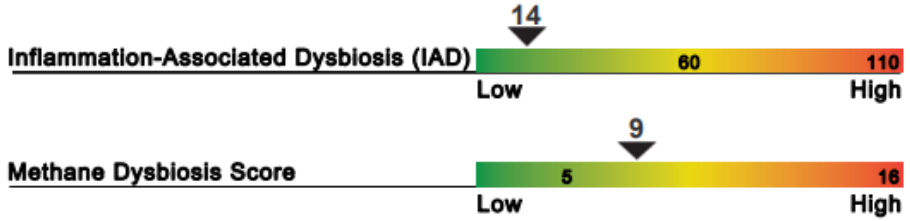
Commensal Microbiome Analysis

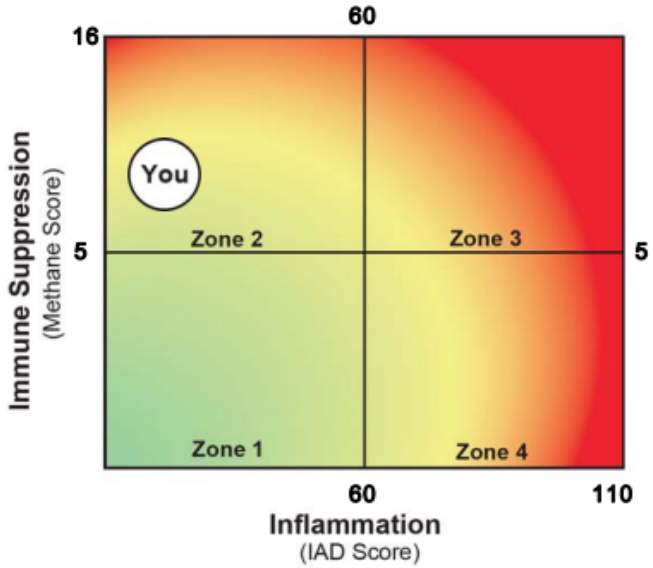
Commensal Abundance



Total Commensal Abundance: The total commensal abundance is a sum-total of the reported commensal bacteria compared to a healthy cohort. Low levels of commensal bacteria are often observed after antimicrobial therapy, or in diets lacking fiber and/or prebiotic-rich foods and may indicate the need for microbiome support. Conversely, higher total commensal abundance may indicate potential bacteria overgrowth or probiotic supplementation.

Dysbiosis Patterns





Dysbiosis Patterns: Genova's data analysis has led to the development of unique dysbiosis patterns, related to key physiologic disruptions, such as immunosuppression and inflammation. These patterns may represent dysbiotic changes that could pose clinical significance. Please see Genova's published literature for more details: https://rdcu.be/bRhzv

Zone 1: The commensal profile in this zone does not align with profiles associated with intestinal inflammation or immunosuppression. If inflammatory biomarkers are present, other causes need to be excluded, such as infection, food allergy, or more serious pathology.

Zone 2: This pattern of bacteria is associated with impaired intestinal barrier function (low fecal sIgA and EPX). Patients in this zone have higher rates of opportunistic infections (e.g. *Blastocystis spp.* & *Dientamoeba fragilis*) as well as fecal fat malabsorption. Commensal abundance is higher in this group suggesting potential bacterial overgrowth.

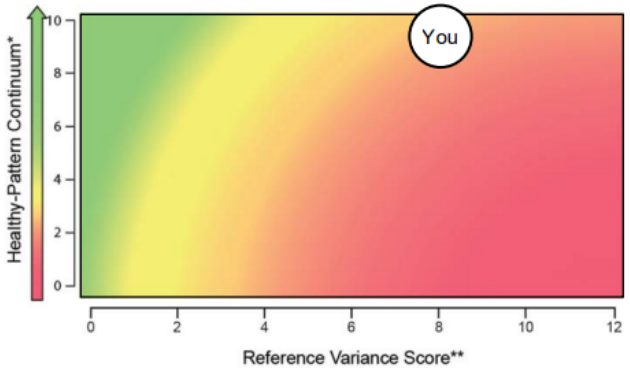
Zone 3: Patients in this zone may have more inflammation compared to those in zone 4. However, commensal abundance is usually higher making use of antimicrobial therapy relatively safer. Patients in this zone may have higher rates of pathogenic infections.

Zone 4: This commensal profile is associated with increased intestinal inflammation. IBD

GENOVA DIAGNOSTICS

Commensal Microbiome Analysis

Commensal Balance

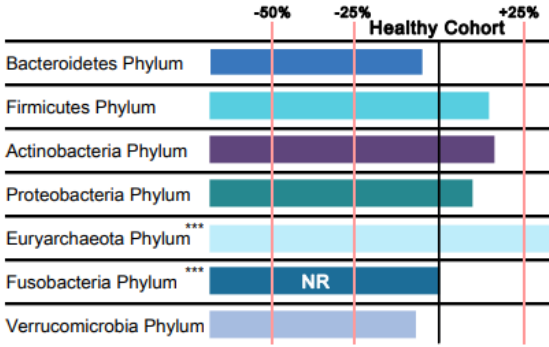


Balanced	Represents 95% of healthy individuals
Borderline	Represents 5% of healthy individuals
Imbalanced	Represents 60% of unhealthy individuals

*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.

**The total number of commensal bacteria (qPCR) that are out of balance for this individual on a scale of 0 to >12.

Relative Commensal Abundance



Increase in *Bacteroides* spp. and *Odoribacter* spp. seen in animal-based diets; *Prevotella* increased with plant-based diet

Contains many butyrate-producers; most species responsive to plant-based diets; *Faecalibacterium* spp. is anti-inflammatory

Bifidobacterium is increased with plant-based diets; *Collinsella* may be proinflammatory, and is elevated with a Western-diet

Some species may be proinflammatory; *E. coli* consumes simple sugars and is lower in individuals on plant-based diets

Methanobrevibacter smithii is associated with methane production and with diets high in carbohydrates

Certain *Fusobacterium* spp. may be proinflammatory and increased on low fiber, high fat diets

Akkermansia spp. is involved in gut membrane integrity and may be increased with polyphenols and prebiotics

Relative Abundance: The relative abundance compares the quantity of each of 7 major bacterial phyla to a healthy cohort. This can indicate broader variances in the patient's gut microbiome profile. Certain interventions may promote or limit individual phyla when clinically appropriate. Please refer to Genova's Stool Testing Support Guide for more information on modulation of commensal bacteria through diet & nutrient interventions. ***Approximately 70% of the healthy cohort had below detectable levels of *Methanobrevibacter smithii*. Approximately 90% of the healthy cohort had below detectable levels of *Fusobacterium spp.*

Physician Notes/Recommendations

2200 GI Effects™ Comprehensive Profile - Stool

Methodology: GC-FID, Automated Chemistry, EIA

	Result	QUINTILE DISTRIBUTION (1st 2nd 3rd 4th 5th)	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 †	139 L	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	8.7		1.8-9.9 micromol/g
Fecal Fat (Total*)	53.5 H		3.2-38.6 mg/g
Triglycerides	1.0		0.3-2.8 mg/g
Long-Chain Fatty Acids	35.4 H		1.2-29.1 mg/g
Cholesterol	3.0		0.4-4.8 mg/g
Phospholipids	14.1 H		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin †	<16	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	0.2	0.5 2.7	<=2.7 mcg/g
Fecal secretory IgA	383	680 2040	<=2,040 mcg/mL
Gut Microbiome Metabolites			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	49.3		>=23.3 micromol/g
n-Butyrate Concentration	7.9		>=3.6 micromol/g
n-Butyrate %	16.0		11.8-33.3 %
Acetate %	65.2		48.1-69.2 %
Propionate %	18.8		<=29.3 %
Beta-glucuronidase	<DL L		368-6,266 U/g

Need for Digestive Support

MALDIGESTION

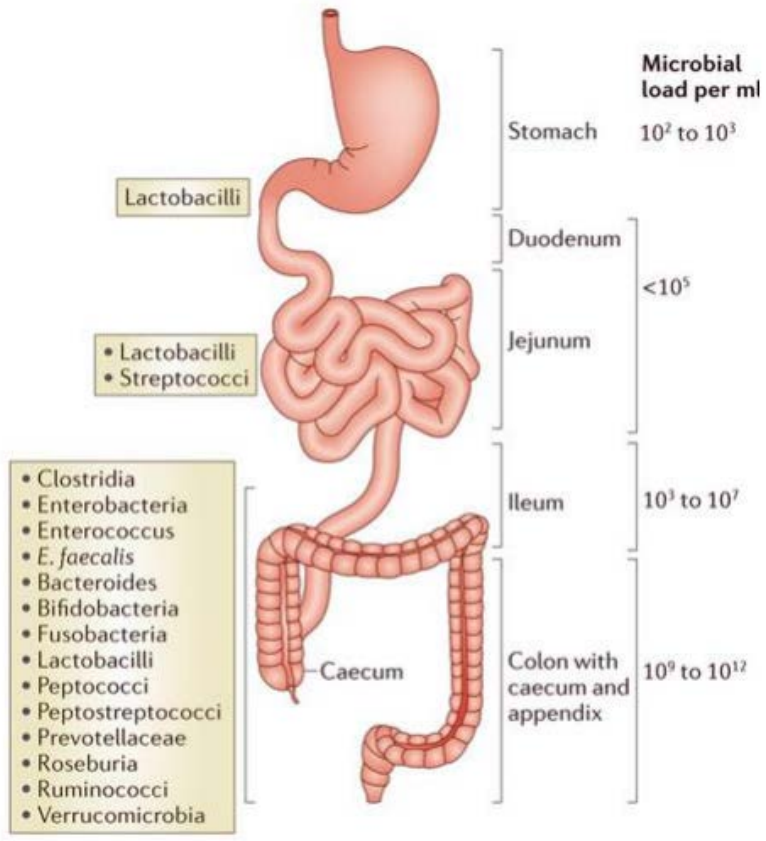
10

- Fecal Fats ▲
- Products of Protein Breakdown △
- Pancreatic Elastase ▽

- Digestive Enzymes
- Betaine HCl
- Bile Salts
- Apple Cider Vinegar
- Mindful Eating Habits
- Digestive Bitters

GENOVA DIAGNOSTICS

Small Intestinal Bacterial Overgrowth (SIBO)



- Mechanical Stasis
  - Structural/anatomic: small intestine diverticula, strictures
- Motility disorders
  - Gastroparesis, hypothyroidism, opioid medications
- Advanced age
- Hypochlorhydria
- PPI's

GENOVA DIAGNOSTICS

Mowat A, et al. Nature Review Immunology. 2014;14(10):667-85.
Dukowicz AC, et al. Gastroenterology and Hepatology. 2007;3(2):112-22.
Martins CP, et al. Arquivos de Gastroenterologia. 2017;54(2):91-95.

SIBO and PE-1

European Journal of Clinical Investigation

European Journal of Clinical Investigation

Fecal elastase-1 is decreased in villous atrophy regardless of the underlying disease

J. Walkow

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Walkowia

27/33, 60

jarwalk@

Subclinical Exocrine Pancreatic Dysfunction Resulting From D Cholecystokinin Secretion in the Presence of Intestinal Villou

Nousia-Arvanitakis. Sanda*: Fotoulaki. Maria*: Tendzidou. Kyriaki*: Vassilaki. Constantina*: Agguridaki. Christina†: Karamou

Author Informatio

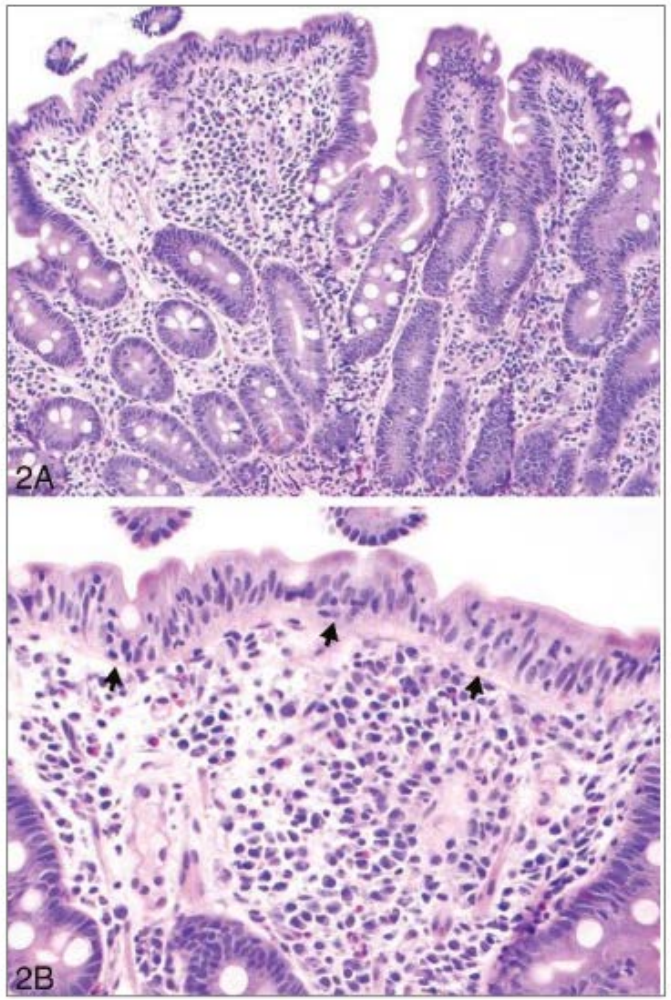
Journal of Pediatr

Small Intestinal Bacterial Overgrowth: Histopathologic Features a Clinical Correlates in an Underrecognized Entity

Paul J. Lappinga, MD; Susan C. Abraham, MD; Joseph A. Murray, MD; Emily A. Vetter, BA; Robin Patel, MD; Tsung-Teh Wu, MD, PhD

Arch Pathol Lab Med (2010) 134 (2): 264–270.

https://doi.org/10.1043/1543-2165-134.2.264 Article history



GENOVA DIAGNOSTICS

Haboubi NY, Lee GS, Montgomery RD. Age Ageing. 1991;20:29-32.
Bures J, et. al. World Journal of Gastroenterology. 2010;16(24):2978-2990.
Lappinga, P, et. al. Arch Pathol Lab Med. 2010;134(2):264-70

Methodology: DNA by qPCR

Gastrointestinal Microbiome (PCR)

Commensal Bacteria (PCR)	Result CFU/g stool	QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Reference Range CFU/g stool
Bacteroidetes Phylum			
Bacteroides uniformis	2.0**E8**		<=9.5**E8**
Phocaeicola vulgatus	<DL		<=8.3**E8**
Barnesiella spp.	1.8**E7**		3.0**E6**-2.9**E8**
Odoribacter spp.	1.0**E7**		<=9.5**E7**
Prevotella spp.	2.9**E8**		6.6**E7**-3.8**E9**
Firmicutes Phylum			
Anaerotruncus colihominis/massiliensis	<DL		<=2.0**E7**
Butyrivibrio crossotus	<DL		<=3.3**E7**
Clostridium spp.	1.6**E7** H		<=1.5**E7**
Coprococcus eutactus	<DL		<=1.2**E8**
Faecalibacterium prausnitzii	7.7**E7**		1.1**E6**-1.1**E9**
Lactobacillus spp.	<DL		<=1.6**E6**
Pseudoflavonifractor spp.	2.4**E6**		1.3**E4**-2.9**E7**
Roseburia spp.	1.4**E7**		3.6**E5**-4.6**E8**
Ruminococcus bromii	8.6**E8**		<=1.5**E9**
Veillonella spp.	3.8**E4**		<=4.1**E6**
Actinobacteria Phylum			
Bifidobacterium spp.	3.4**E8** H		4.6**E5**-2.6**E8**
Bifidobacterium longum subsp. longum	1.1**E8**		<=1.3**E8**
Collinsella aerofaciens	1.4**E8** H		<=1.3**E8**
Proteobacteria Phylum			
Desulfovibrio piger	<DL		<=5.4**E7**
Escherichia coli	1.1**E7** H		<=7.5**E6**
Oxalobacter formigenes	<DL		<=1.1**E7**
Euryarchaeota Phylum			
Methanobrevibacter smithii	2.6**E7** H		<=2.0**E7**
Fusobacteria Phylum			
Fusobacterium spp.	<DL		<=1.8**E5**
Verrucomicrobia Phylum			
Akkermansia muciniphila	1.3**E6**		>=8.5**E3**

GENOVA DIAGNOSTICS

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

Gastrointestinal Microbiome (Culture)

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

Microbiology Legend

NG	NP	PP	Pa
No Growth	Non-Pathogen	Potential Pathogen	

Bacteriology (Culture)

Lactobacillus spp.

Escherichia coli

Bifidobacterium (Anaerobic Culture)

Additional Bacteria

Salmonella spp.

Shigella spp.

Mycology (Culture)

Parasitology

Microscopic O&P Results

Microscopic O&P is capable of detect
commonly found in microscopic stool
in the Additional Results section. The
reference of all potentially detectable

Genus/species
Nematodes - roundworms
Ancylostoma/Necator (Hookworm)
Ascaris lumbricoides
Capillaria philippinensis
Enterobius vermicularis
Strongyloides stercoralis
Trichuris trichiura
Cestodes - tapeworms
Diphyllobothrium latum
Dipylidium caninum
Hymenolepis diminuta
Hymenolepis nana
Taenia spp.
Trematodes - flukes
Clonorchis/Opisthorchis spp.
Fasciola spp./ *Fasciolopsis buski*
Heterophyes/Metagonimus
Paragonimus spp.
Schistosoma spp.
Protozoa
Balantidium coli
Blastocystis spp.
Chilomastix mesnili
Cryptosporidium spp.
Cyclospora cayetanensis
Dientamoeba fragilis
Entamoeba coli
Entamoeba histolytica/dispar
Entamoeba hartmanii
Entamoeba polecki
Endolimax nana
Giardia
Iodamoeba buetschlii
Cystoisospora spp.
Trichomonads (e.g. *Pentatrichomonas*
Additional Findings
White Blood Cells
Charcot-Leyden Crystals
Other Infectious Findings

Parasitology

PCR Parasitology - Protozoa

Methodologies: DNA by PCR

Organism	Result	Units		Expected Result
Blastocystis spp.	<2.14e2	femtograms/microliter C&S stool	Not Detected	Not Detected
Cryptosporidium parvum/hominis	<1.76e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Cyclospora cayetanensis	<2.65e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Dientamoeba fragilis	<1.84e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Entamoeba histolytica	<9.64e1	genome copies/microliter C&S stool	Not Detected	Not Detected
Giardia	<1.36e1	genome copies/microliter C&S stool	Not Detected	Not Detected

Additional Results

Methodology: Fecal Immunochemical Testing (FIT)

	Result	Expected Value
Fecal Occult Blood◆	Negative	Negative
Consistency††	Hard/Constip.	

††Results provided from patient input.

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.

GENOVA DIAGNOSTICS

Case Study #1 – Summary and Next Steps

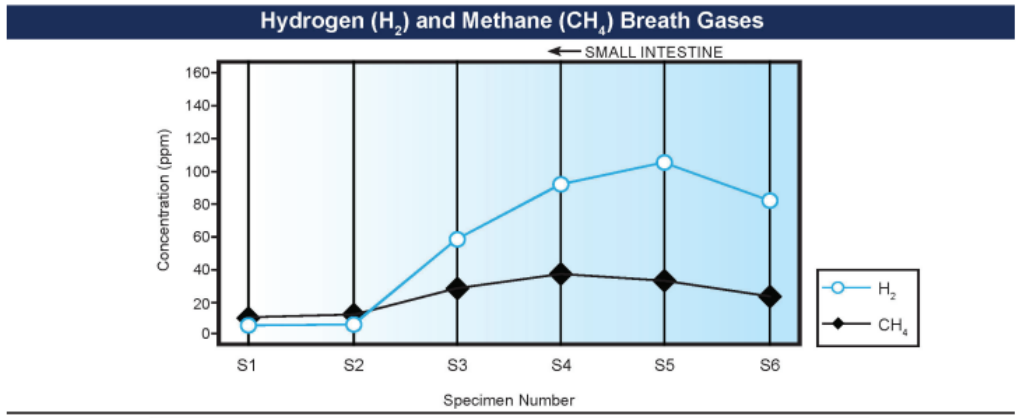
- High Score in Maldigestion and Dysbiosis Pillars
- Trending commensal abundance and Methane Dysbiosis score
- Low Pancreatic Elastase with high PPB and Fecal Fats

- Hx IBS
- Bloating, constipation/diarrhea
- Weight gain

- Possible Small Intestinal Bacterial Overgrowth (SIBO)? – Now what?

GENOVA DIAGNOSTICS

SIBO Breath Testing



Hydrogen (H_2), Methane (CH_4) and Carbon Dioxide (CO_2) (ppm)						
	Baseline 0 min (S1)	20 min (S2)	40 min (S3)	60 min (S4)	90 min (S5)	120 min (S6)
H_2	4	7	59	97	106	76
CH_4	10	12	28	38	35	26
H_2 + CH_4	14	19	87	135	141	102
CO_2**	✓	✓	✓	✓	✓	✓
Actual Collection Times						
Actual Time	9:55	10:17	10:39	11:00	11:30	12:00
Actual Interval	0 min	22 min	44 min	65 min	95 min	125 min

**CO_2 is measured for quality assurance. ✓ indicates the CO_2 level is acceptable. X indicates room air contamination exceeding acceptable limits.

Evaluation for Hydrogen (H_2)		
Hydrogen increase over baseline by 90 minutes		
	Result	Expected Value
Change in H_2	102	H < 20 ppm

A rise ≥ 20 ppm from baseline in hydrogen by 90 min should be considered a positive test to suggest the presence of SIBO.

Evaluation for Methane (CH_4)		
Peak methane level at any point		
	Result	Expected Value
CH_4 Peak	38	H < 10 ppm

A peak methane level ≥ 10 ppm at any point is indicative of a methane-positive result.

- Rise of H2 ≥ 20 ppm over baseline by 90 minutes +SIBO
- Peak Level of CH4 ≥ 10 ppm at any point +IMO

GENOVA DIAGNOSTICS

Rezaie A, Buresi M, Lembo A, et al. Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus. American Journal of Gastroenterology. May 2017;112(5):775-784.

Takakura, W., & Pimentel, M. (2020). Small Intestinal Bacterial Overgrowth and Irritable Bowel Syndrome – An Update. *Frontiers in Psychiatry*, *11*, 558965

Treatment

- Dr. Alison Siebecker
  - https://www.siboinfo.com/

Herbal Antibiotics

Like pharmaceutical antibiotics, this a
antibiotics (HAbx). It is the first choi
followed with preventative measures.
effective as Rifaximin" with "similar r
peppermint oil (ECPO), in a single pa
since 2011. We have consistently four
levels on breath testing.

Which ones are used?

Numerous herbs demonstrate antibio
dose is crucial. Because there have or
pharmaceutical antibiotics.

The Multi-Center Team used:
2 herbal combination formulas togeth
Biotics FC Cidal with Biotics Dysbi
Metagenics Candibactin-AR with M

My team commonly uses:
1-3 of the following herbs x 4 weeks p
Allicin from Garlic (the highest pote
Oregano
Berberine- found in Goldenseal, Or
Neem
Cinnamon

Antibiotic Treatment

This approach seeks to attack the bacterial overgrowth head on and fairly quickly with antibiotic drugs (Abx). It is the first choice for most gastroenterologists. It must be followed with preventative measures. Dose finding studies have achieved up to 91% success in eradicating SIBO (measured by hydrogen breath test) and 94% symptom improvement.

Which ones are used?

The primary antibiotics used are Rifaximin (Xifaxan) and Neomycin. They are almost completely non-absorbable which means they stay in the intestines, having a local action and don't cause systemic side effects, such as urinary tract infections. They are chosen specifically for this property which allows them to act only where they are needed. Metronidazole, a systemic antibiotic, is also used.

SIBO Antibiotic Doses

The following information is provided for physicians, based on the most recent dose finding studies and clinical expertise of Drs Scarpellini, Pimentel, Lombardo, Furnari and their teams. Many thanks for all their excellent, tireless work.

- Rifaximin may be used for all cases of SIBO. There are 3 excellent dose options currently reported.
- Neomycin is effective for constipation cases and is used in addition to Rifaximin, as double Abx therapy. Metronidazole is an effective alternative to Neomycin, currently under study at Cedars-Sinai.
- If alternating diarrhea is present with constipation, the use of Rifaximin alone has been suggested.

Rifaximin Dose Options:
1) 1600 mg per day x 10 days- 70-85% success normalizing LBT, 82% success normalizing GBT (Scarpellini)
   1650 mg per day x 14 days (Pimentel), 550 mg tid.
2) 1200 mg per day x 14 days- 87-91% success normalizing GBT, 90-94% symptom improvement (Lombardo)
3) 1200 mg per day x 10 days with 5 g per day Partially Hydrolyzed Guar Gum
   -87% success normalizing GBT, 91% symptom improvement (Furnari)

Rifaximin is available in both 200 mg and 550 mg in the US. Tid study doses are given at 8 am, 2 pm, 8 pm.

Rifaximin Pediatric Dosing:
1) 600mg per day x 7 days - 64% success normalizing LBT (Scarpellini)
2) 10-30mg/kg body weight, for IBD. 61% of cases had symptom relief. Higher dose had better pain relief. (Muniyappa)

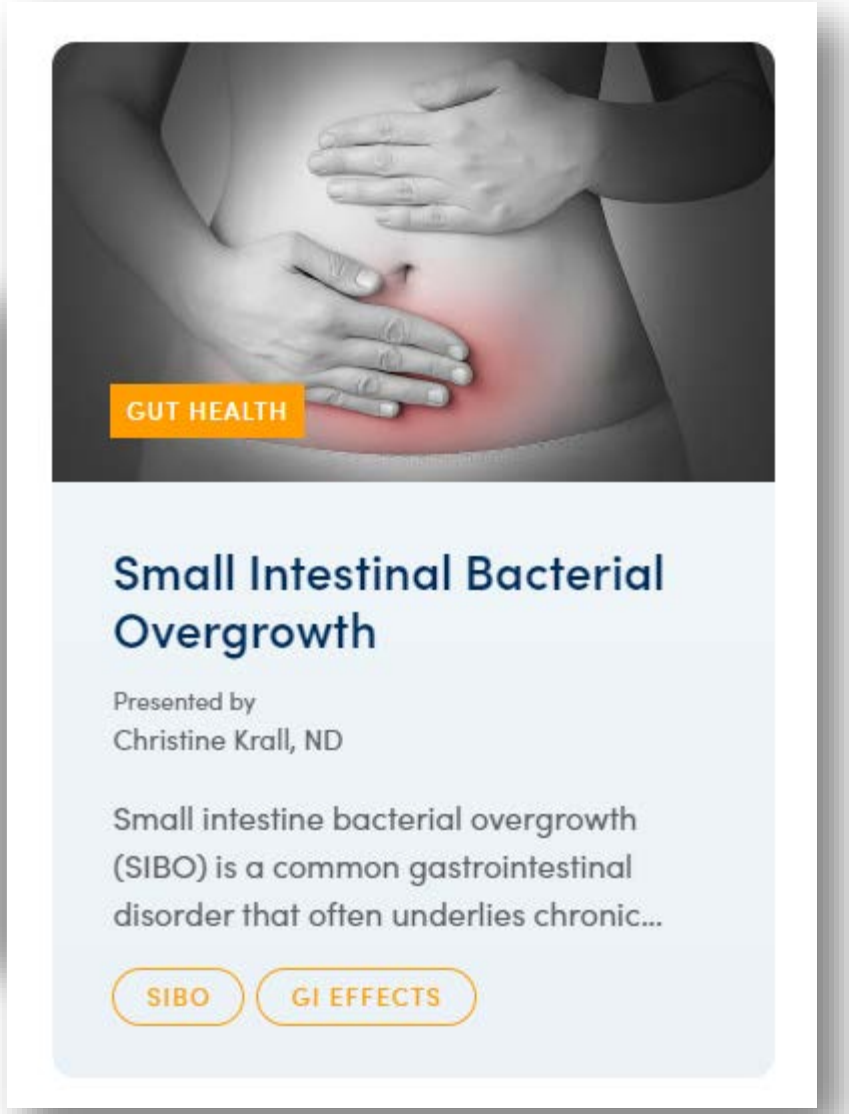
Rifaximin + Neomycin Dosing:
Rifaximin 1600 mg per day + Neomycin 1000 mg per day x 10 days, 87% success normalizing LBT (Pimentel- this study used 1200 mg Rifaximin x 10 days but Dr Pimentel currently uses 1650 mg/day).

Neomycin is available in 500 mg in the US and is given bid (8 am and 8 pm or as fits one's schedule).

GENOVA DIAGNOSTICS

Treatment – Root cause

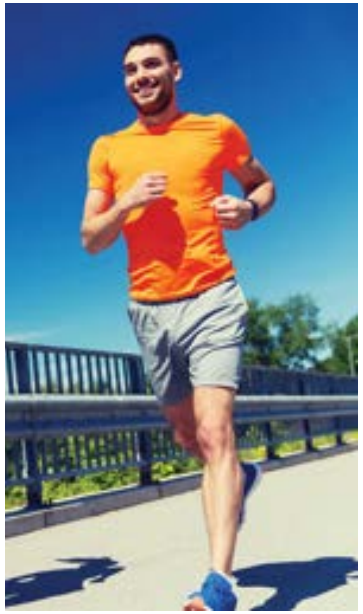
- Genova's Learning Library
  - https://gdx.net/education/



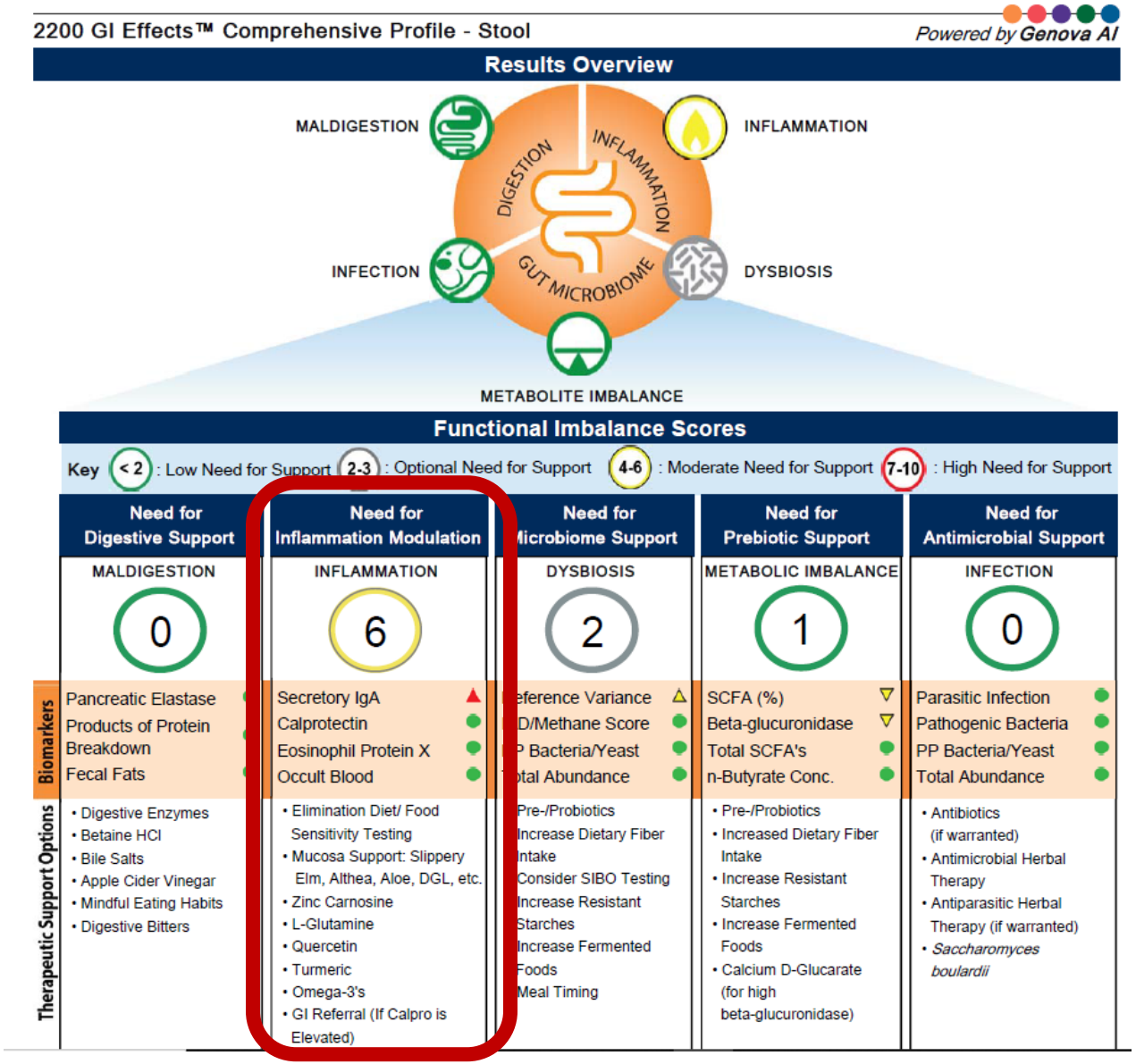
GENOVA DIAGNOSTICS

Case Study #2

- 17 yr. old male
- Long-distance runner – track & field team
- No PMHx
- No medications
- Standard American Diet – though higher protein



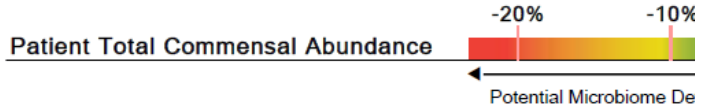
- Frequent diarrhea
- Joint pain



GENOVA DIAGNOSTICS

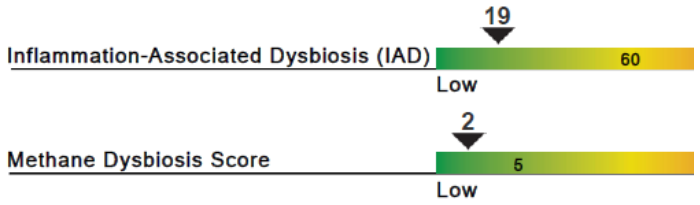
Commensal Microbiome Analysis

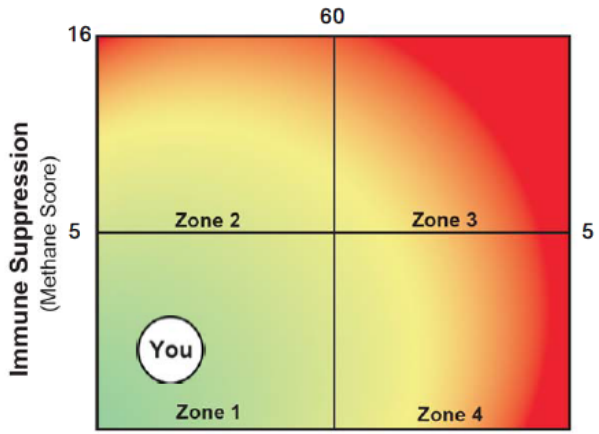
Commensal Abundance



Total Commensal Abundance: The total commensal abundance is a sum-tota healthy cohort. Low levels of commensal bacteria are often observed after antimi prebiotic-rich foods and may indicate the need for microbiome support. Converse potential bacteria overgrowth or probiotic supplementation.

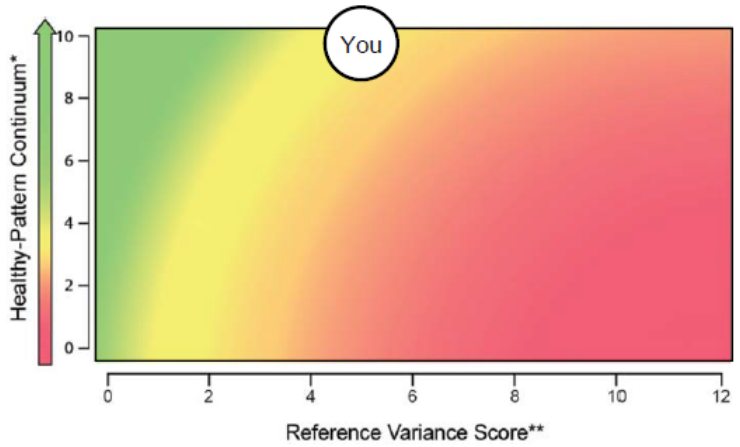
Dysbiosis Patterns





Commensal Microbiome Analysis

Commensal Balance

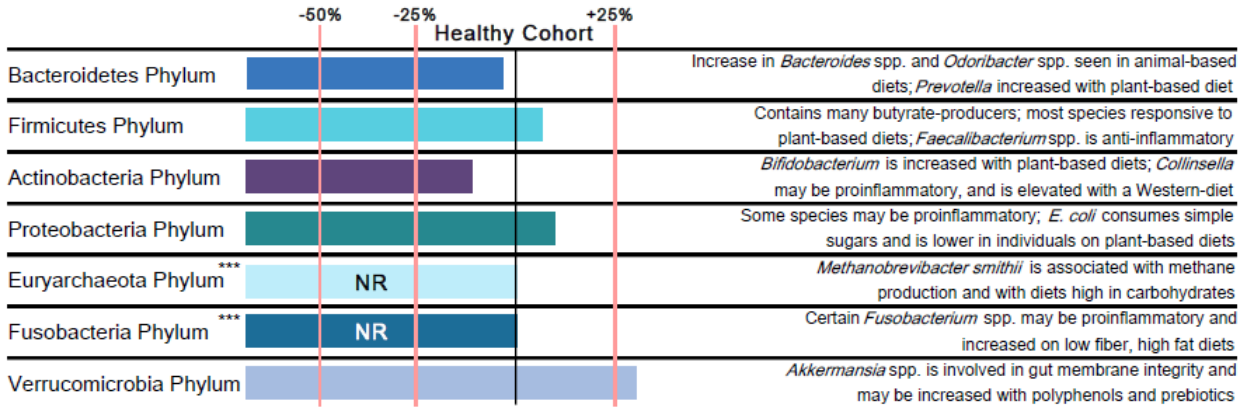


Balanced	Represents 95% of healthy individuals
Borderline	Represents 5% of healthy individuals
Imbalanced	Represents 60% of unhealthy individuals

*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.

**The total number of commensal bacteria (qPCR) that are out of balance for this individual on a scale of 0 to >12.

Relative Commensal Abundance



Relative Abundance: The relative abundance compares the quantity of each of 7 major bacterial phyla to a healthy cohort. This can indicate broader variances in the patient's gut microbiome profile. Certain interventions may promote or limit individual phyla when clinically

2200 GI Effects™ Comprehensive Profile - Stool

Methodology: GC-FID, Automated Chemistry, EIA

	Result	QUINTILE DISTRIBUTION (1st 2nd 3rd 4th 5th)	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 †	>500	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	3.2		1.8-9.9 micromol/g
Fecal Fat (Total*)	17.9		3.2-38.6 mg/g
Triglycerides	0.8		0.3-2.8 mg/g
Long-Chain Fatty Acids	10.3		1.2-29.1 mg/g
Cholesterol	6.2 H		0.4-4.8 mg/g
Phospholipids	0.6		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin †	<17	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	0.1	0.5 2.7	<=2.7 mcg/g
Fecal secretory IgA	>7500 H	680 2040	<=2,040 mcg/mL
Gut Microbiome Metabolites			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	48.8		>=23.3 micromol/g
n-Butyrate Concentration	7.3		>=3.6 micromol/g
n-Butyrate %	15.0		11.8-33.3 %
Acetate %	57.0		48.1-69.2 %
Propionate %	27.9		<=29.3 %
Beta-glucuronidase	647		368-6,266 U/g

Need for Inflammation Modulation

INFLAMMATION

6

- Secretory IgA
- Calprotectin
- Eosinophil Protein X
- Occult Blood

- Elimination Diet/ Food Sensitivity Testing
- Mucosa Support: Slippery Elm, Althea, Aloe, DGL, etc.
- Zinc Carnosine
- L-Glutamine
- Quercetin
- Turmeric
- Omega-3's
- GI Referral (If Calpro is Elevated)

GENOVA DIAGNOSTICS

Methodology: DNA by qPCR

Gastrointestinal Microbiome

Commensal Bacteria (PCR)

Result CFU/g stool | 1st | 2nd QUINTIL

Bacteroidetes Phylum
- *Bacteroides uniformis*
- *Phocaeicola vulgatus*
- *Barnesiella spp.*
- *Odoribacter spp.*
- *Prevotella spp.*

Firmicutes Phylum
- *Anaerotruncus colihominis/massiliensis*
- *Butyrivibrio crossotus*
- *Clostridium spp.*
- *Coprococcus eutactus*
- *Faecalibacterium prausnitzii*
- *Lactobacillus spp.*
- *Pseudoflavonifractor spp.*
- *Roseburia spp.*
- *Ruminococcus bromii*
- *Veillonella spp.*

Actinobacteria Phylum
- *Bifidobacterium spp.*
- *Bifidobacterium longum subsp. long*
- *Collinsella aerofaciens*

Proteobacteria Phylum
- *Desulfovibrio piger*
- *Escherichia coli*
- *Oxalobacter formigenes*

Euryarchaeota Phylum
- *Methanobrevibacter smithii*

Fusobacteria Phylum
- *Fusobacterium spp.*

Verrucomicrobia Phylum
- *Akkermansia muciniphila*

Methodology: Culture/MALDI-TOF MS, Autom

Human microflora is influenced by e
competitive ecosystem of the organ
significance should be based upon

Microbiolog

NG	NP
☐ No Growth	☐ Non-Pathogen

Bacteriology (Culture)

- *Lactobacillus spp.*
- *Escherichia coli*
- *Bifidobacterium (Anaerobic Culture)*

Additional Bacteria

- *Salmonella spp.*
- *Shigella spp.*
- *Enterococcus faecium*

Mycology (Culture)

Parasitology

Microscopic O&P Results

Microscopic O&P is capable of detecting all c
commonly found in microscopic stool analysi
in the Additional Results section. These resul
reference of all potentially detectable organis

Genus/species	
Nematodes - roundworms	
Ancylostoma/Necator (Hookworm)	
Ascaris lumbricoides	
Capillaria philippinensis	
Enterobius vermicularis	
Strongyloides stercoralis	
Trichuris trichiura	
Cestodes - tapeworms	
Diphyllobothrium latum	
Dipylidium caninum	
Hymenolepis diminuta	
Hymenolepis nana	
Taenia spp.	
Trematodes - flukes	
Clonorchis/Opisthorchis spp.	
Fasciola spp./ Fasciolopsis buski	
Heterophyes/Metagonimus	
Paragonimus spp.	
Schistosoma spp.	
Protozoa	
Balantidium coli	
Blastocystis spp.	
Chilomastix mesnili	
Cryptosporidium spp.	
Cyclospora cayetanensis	
Dientamoeba fragilis	
Entamoeba coli	
Entamoeba histolytica/dispar	
Entamoeba hartmanii	
Entamoeba polecki	
Endolimax nana	
Giardia	
Iodamoeba buetschlii	
Cystoisospora spp.	Not Detected
Trichomonads (e.g. Pentatrichomonas)	Not Detected
Additional Findings	
White Blood Cells	Not Detected
Charcot-Leyden Crystals	Not Detected
Other Infectious Findings	

Parasitology

PCR Parasitology - Protozoa

Methodologies: DNA by PCR

Organism	Result	Units		Expected Result
Blastocystis spp.	<2.14e2	femtograms/microliter C&S stool	Not Detected	Not Detected
Cryptosporidium parvum/hominis	<1.76e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Cyclospora cayetanensis	<2.65e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Dientamoeba fragilis	<1.84e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Entamoeba histolytica	<9.64e1	genome copies/microliter C&S stool	Not Detected	Not Detected
Giardia	<1.36e1	genome copies/microliter C&S stool	Not Detected	Not Detected

Additional Results

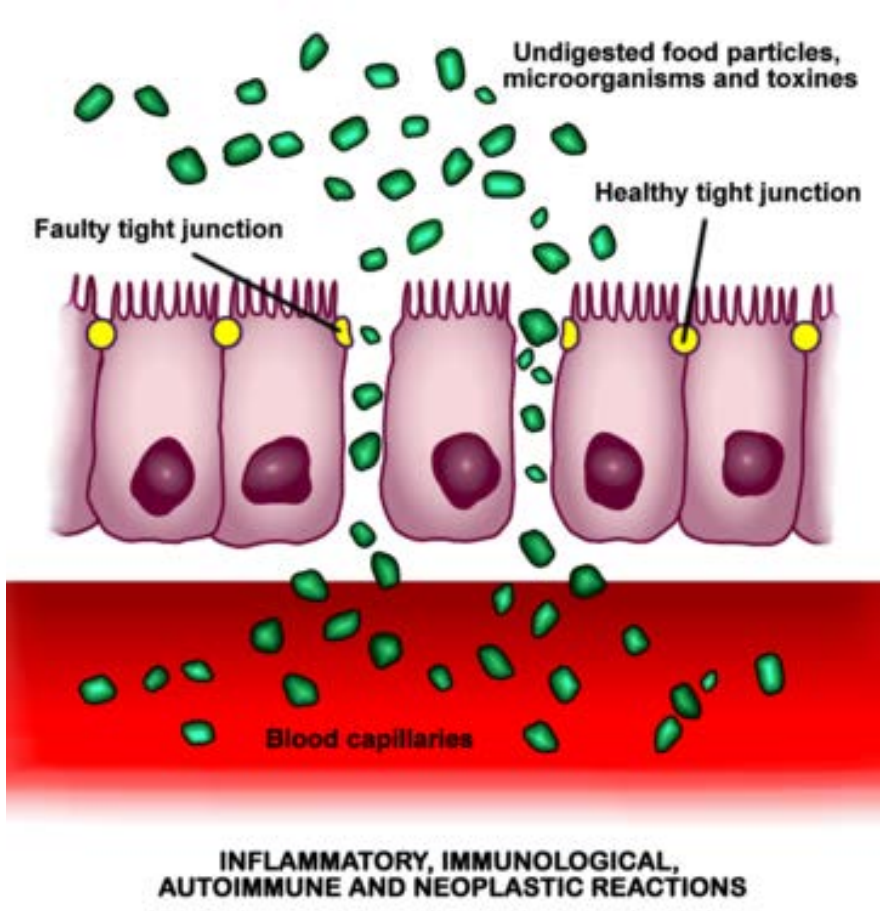
Methodology: Fecal Immunochemical Testing (FIT)

	Result	Expected Value
Fecal Occult Blood•	Negative	Negative
Color††	Brown	
Consistency††	Hard/Constip.	

††Results provided from patient input.
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.

GENOVA DIAGNOSTICS

Intestinal Permeability



- Food Sensitivities
- Gluten
- Alcohol
- NSAID use
- Prolonged or strenuous exercise
- Stress
- Inflammation – IBD, infection

GENOVA DIAGNOSTICS

Resnick C .Natural Medicine Journal .Jan.2014;

Case Study #2 – Summary and Next Steps

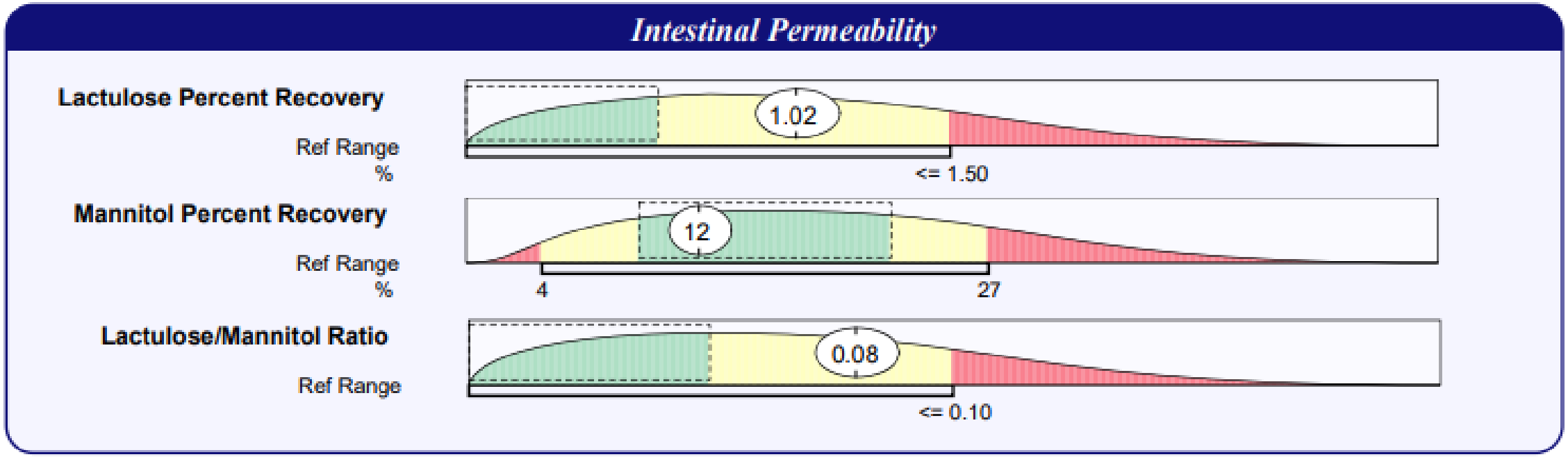
- Elevated fecal secretory IgA
- No pathogens or potential pathogens

- Intermittent diarrhea
- Join pain

- Possible Intestinal Permeability– Now what?

GENOVA DIAGNOSTICS

Intestinal Permeability Assessment



GENOVA DIAGNOSTICS

Treatment

- Herbal supplementation
  - Slippery elm, aloe, marshmallow root
- L-glutamine
- Quercetin
- Pre- and probiotics
- Low FODMAP diet – reduce dietary fats/sugar
- Fiber
- Antioxidants (NAC, Vit C and E)
- Phosphatidylcholine
- Dihomo-gamma- linolenic and Gamma-linolenic acid

- MOST IMPORTANTLY - Investigate and correct the underlying cause……

GENOVA DIAGNOSTICS

Resnick C .Natural Medicine Journal .Jan.2014; https://www.naturalmedicinejournal.com/journal/nutritional-protocol-treatment-intestinal-permeability-defects-and-related
Aleman RS, et.al. Molecules. 2023;28(2), 619
Paray BA, et.al. International Journal of Molecular Sciences. 2020,21,9770

Celiac Profile

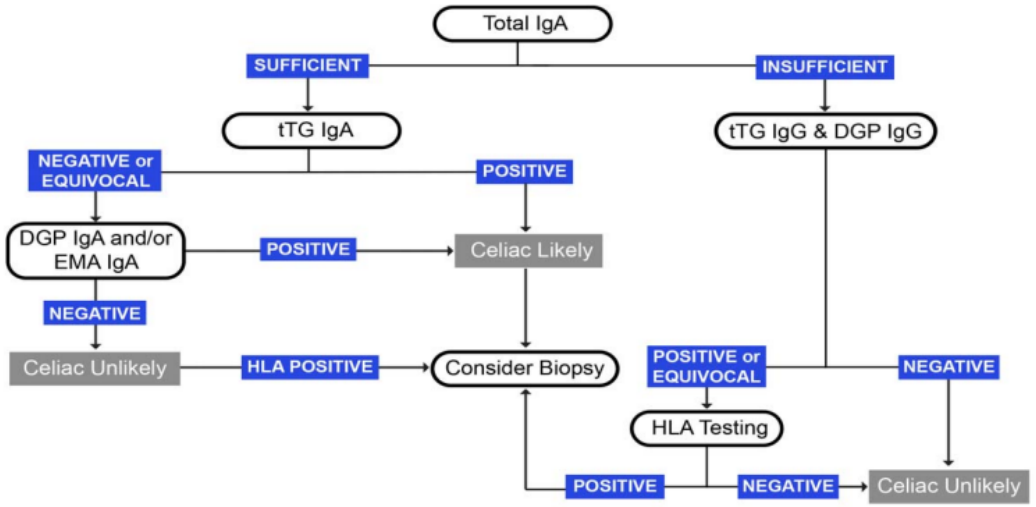
1018 Celiac Profile - Serum

Methodology: FEIA, Immunoturbidometric and IFA (when EMA IgA testing is performed)

Immunologic Markers

Biomarker	Result		Reference Range
Total IgA	394	Sufficient	85-532 mg/dL
Anti-Tissue Transglutaminase IgG (tTG IgG)	<1.7	Negative	<=6.9 U/ml
Anti-Deamidated Gliadin IgG (DGP IgG)	<1.4	Negative	<=6.9 U/ml
Anti-Tissue Transglutaminase IgA (tTG IgA)	0.7	Negative	<=6.9 U/ml
Anti-Deamidated Gliadin IgA (DGP IgA)	4.8	Negative	<=6.9 U/ml

Interpretation



GENOVA DIAGNOSTICS

IgG Food Antibody Testing

1001 IgG Food Antibodies Profile - Serum

Methodology: EIA and Chemiluminescent

IgG Food Antibody Results

Dairy

Casein	VL
Cheddar cheese	VL
Cottage cheese	VL
Cow's milk	1+
Goat's milk	0
Lactalbumin	VL
Yogurt	1+

Fruits

Apple	0
Apricot	0
Banana	0
Blueberry	0
Cranberry	0
Grape	VL
Grapefruit	0
Lemon	0
Orange	0
Papaya	0
Peach	VL
Pear	0
Pineapple	1+
Plum	0
Raspberry	0
Strawberry	0

Vegetables

Alfalfa	0
Asparagus	VL
Avocado	0
Beets	0
Broccoli	VL
Cabbage	0
Carrot	0
Celery	0
Cucumber	0
Garlic	1+
Green Pepper	0
Lettuce	0
Mushroom	0
Olive	0
Onion	0
Pea	0
Potato, sweet	0
Potato, white	VL
Spinach	VL
String bean	VL
Tomato	VL
Zucchini	0

Fish/Shellfish

Clam	0
Cod	0
Crab	0
Lobster	0
Oyster	0
Red snapper	0
Salmon	0
Sardine	0
Shrimp	0
Sole	0
Trout	0
Tuna	0

Poultry/Meats

Beef	0
Chicken	0
Egg white	0
Egg yolk	0
Lamb	0
Pork	0
Turkey	0

Nuts and Grains

Almond	VL
Buckwheat	VL
Corn	0
Corn gluten	1+
Gluten	3+
Kidney bean	VL
Lentil	0
Lima bean	0
Oat	0
Peanut	0
Pecan	0
Pinto bean	0
Rice	VL
Rye	0
Sesame	3+
Soy	VL
Sunflower seed	3+
Walnut	VL
Wheat	3+

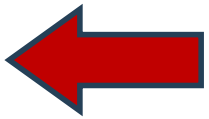
Miscellaneous

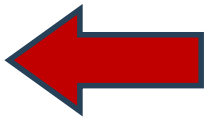
Yeast	VL
Cane sugar	VL
Chocolate	VL
Coffee	3+

Total IgE

	Inside	Outside	Reference Range
Total IgE ◆	9.2		<=87.0 IU/mL

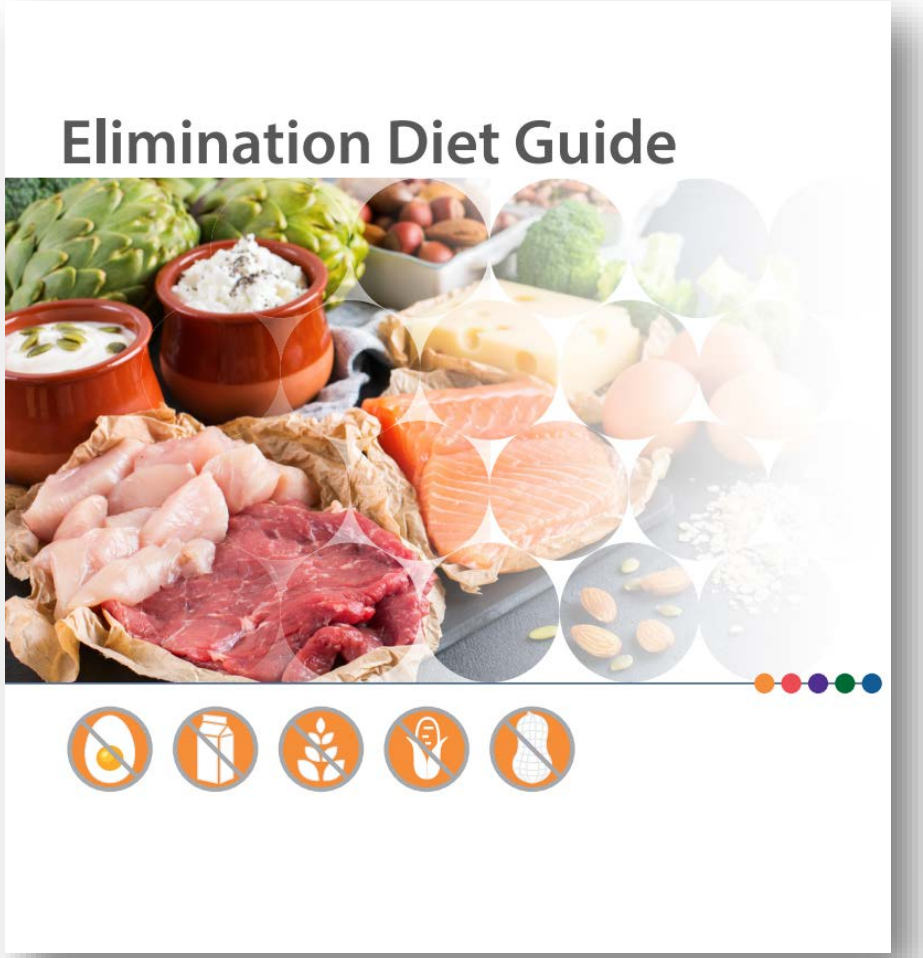
0 None Detected VL Very Low 1+ Low 2+ Moderate 3+ High





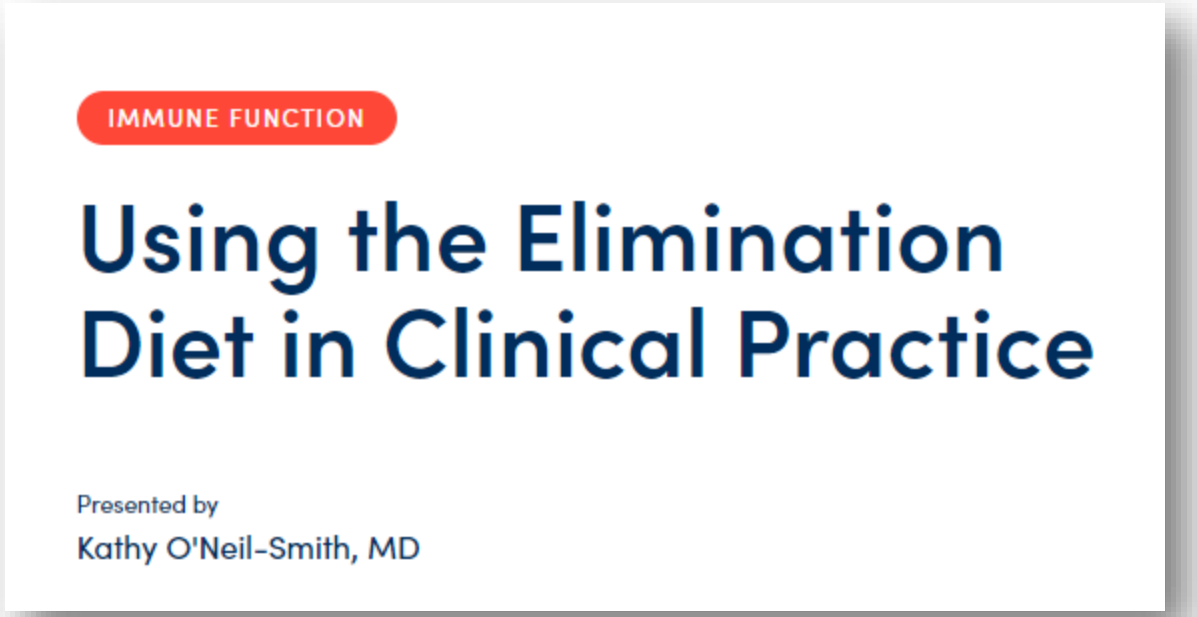
GENOVA DIAGNOSTICS

Elimination Diet



Genova's Learning Library

- https://www.gdx.net/education/

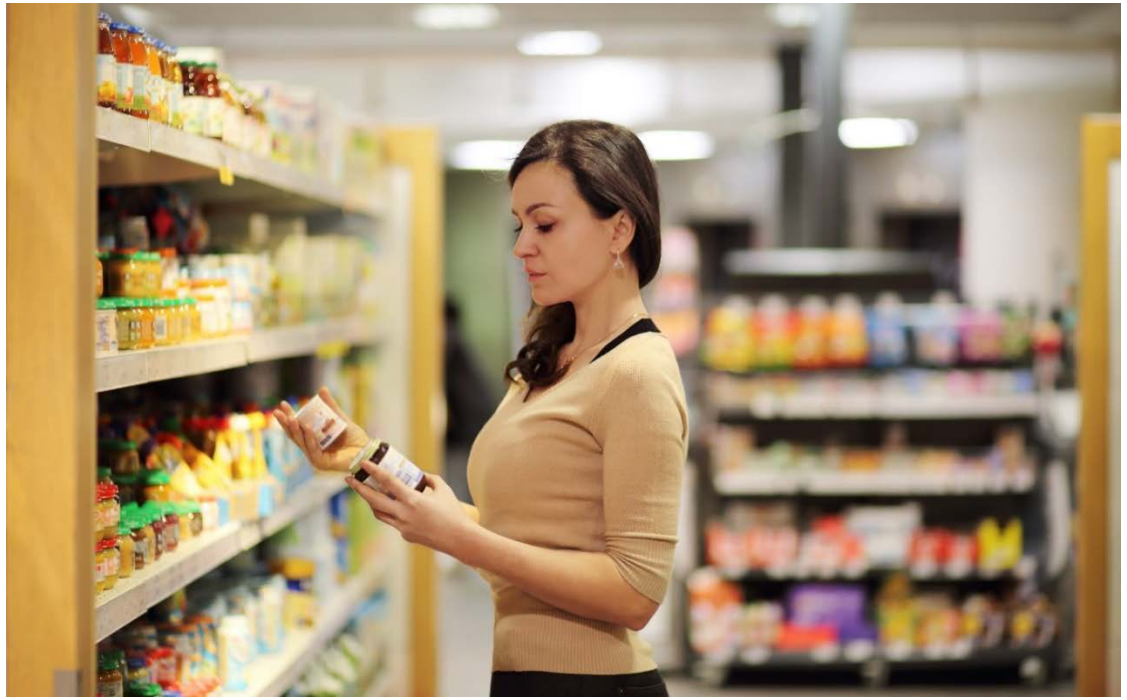


GENOVA DIAGNOSTICS

Case Study #3

- 30 yr. old female
- No PMx, No Medications
- Standard American Diet
- Wine each evening after work

- Brain fog
- Fatigue
- Occasional diarrhea

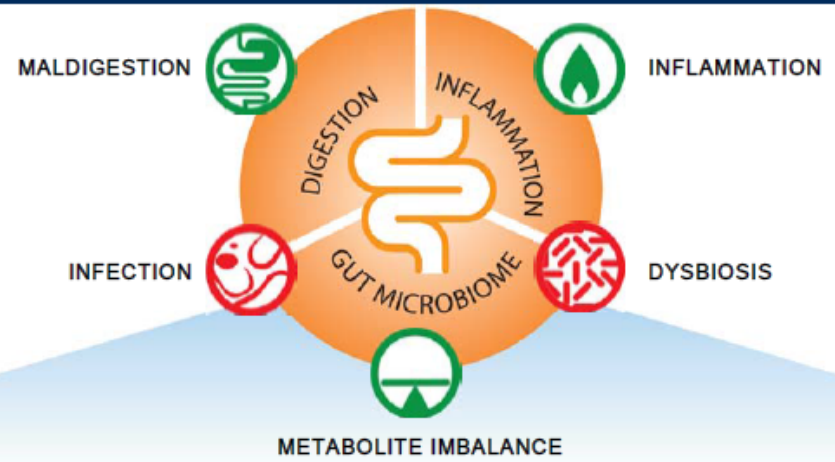


GENOVA DIAGNOSTICS

2200 GI Effects™ Comprehensive Profile - Stool

Powered by Genova AI

Results Overview



Functional Imbalance Scores

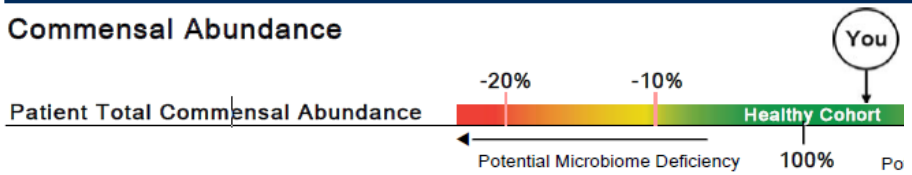
Key (< 2) : Low Need for Support (2-3) : Optional Need for Support (4-6) : Moderate Need for Support (7-10) : High Need for Support

	Need for Digestive Support	Need for Inflammation Modulation	Need for Microbiome Support	Need for Prebiotic Support	Need for Antimicrobial Support
	MALDIGESTION	INFLAMMATION	DYSBIOSIS	METABOLIC IMBALANCE	INFECTION
	1	0	7	0	10
Biomarkers	Products of Protein Breakdown △	Calprotectin ●	PP Bacteria/Yeast ▲	Total SCFA's ●	Parasitic Infection ▲
	Pancreatic Elastase ●	Eosinophil Protein X ●	IAD/Methane Score △	n-Butyrate Conc. ●	PP Bacteria/Yeast ▲
	Fecal Fats ●	Secretory IgA ●	Reference Variance ●	SCFA (%) ●	Pathogenic Bacteria ●
		Occult Blood ●	Total Abundance ●	Beta-glucuronidase ●	Total Abundance ●

GENOVA DIAGNOSTICS

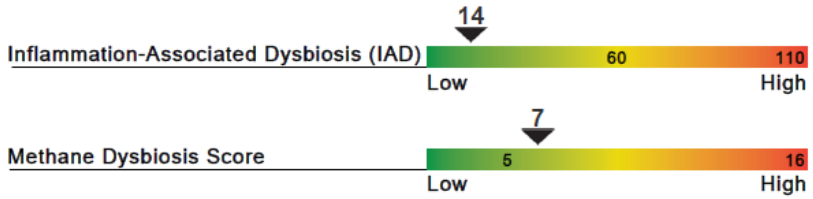
Commensal Microbiome Analysis

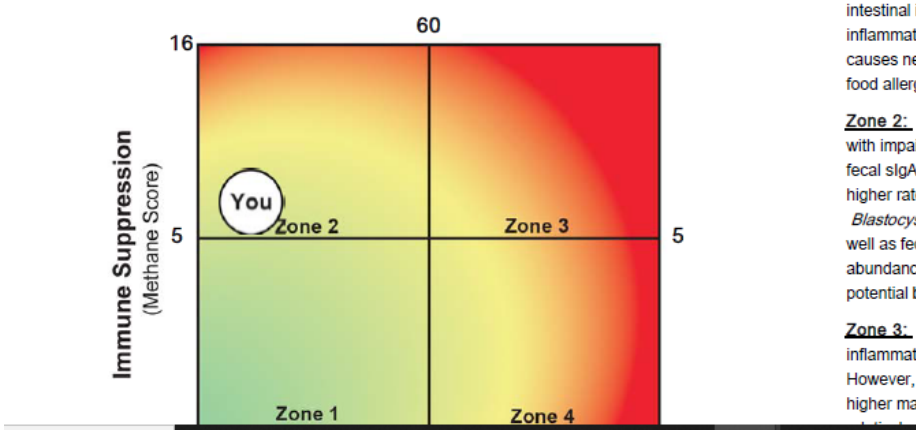
Commensal Abundance



Total Commensal Abundance: The total commensal abundance is a sum-total of the reported commensa
healthy cohort. Low levels of commensal bacteria are often observed after antimicrobial therapy, or in diets la
prebiotic-rich foods and may indicate the need for microbiome support. Conversely, higher total commensal a
potential bacteria overgrowth or probiotic supplementation.

Dysbiosis Patterns





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Zone 3:
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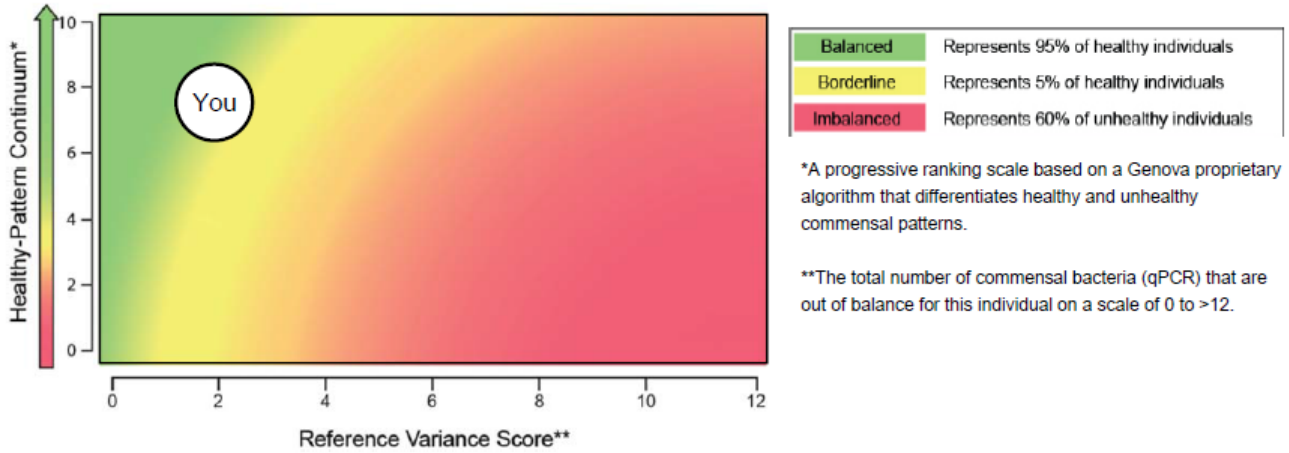
higher ma

Commensal Microbiome Analysis

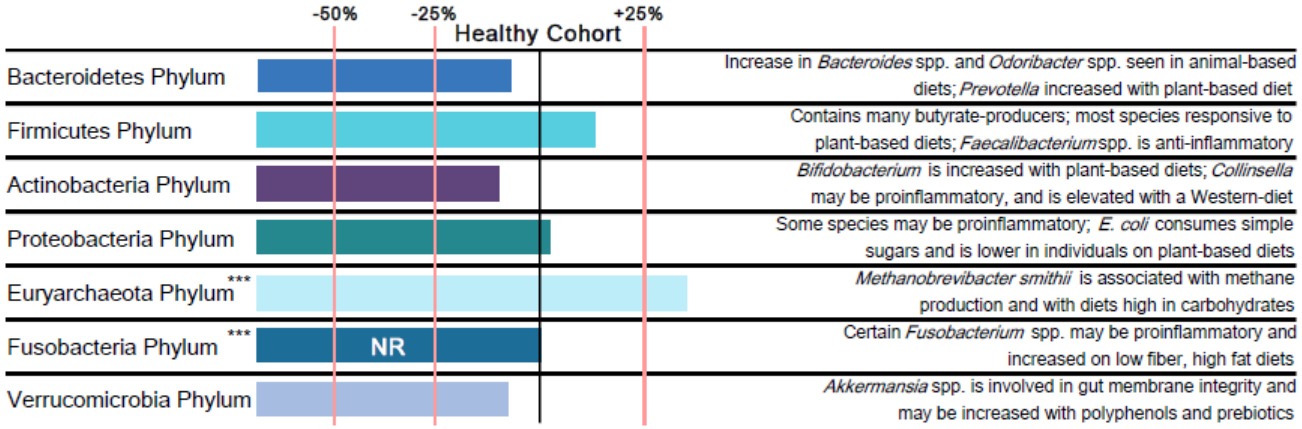
Commensal Balance



*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.

**The total number of commensal bacteria (qPCR) that are out of balance for this individual on a scale of 0 to >12.

Relative Commensal Abundance



Relative Abundance: The relative abundance compares the quantity of each of 7 major bacterial phyla to a healthy cohort. This can

GENOVA DIAGNOSTICS

2200 GI Effects™ Comprehensive Profile - Stool

Methodology: GC-FID, Automated Chemistry, EIA

	Result	QUIN 1st 2nd
Digestion and Absor		
Pancreatic Elastase 1 †	326	100
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	7.5	
Fecal Fat (Total*)	13.0	
Triglycerides	0.4	
Long-Chain Fatty Acids	10.0	
Cholesterol	0.5	
Phospholipids	2.1	
Inflammation and Immu		
Calprotectin †	<16	50
Eosinophil Protein X (EPX)†	0.3	0.5
Fecal secretory IgA	440	680
Gut Microbiome Metab		
Metabolic		
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	48.9	
n-Butyrate Concentration	9.4	
n-Butyrate %	19.2	
Acetate %	58.1	
Propionate %	22.7	
Beta-glucuronidase	1,856	

Methodology: DNA by qPCR

Gastrointestinal Microbiome (PCR)

Commensal Bacteria (PCR)	Result CFU/g stool	QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th	Reference Range CFU/g stool
Bacteroidetes Phylum			
Bacteroides uniformis	3.1E7		<=9.5E8
Phocaeicola vulgatus	4.3E7		<=8.3E8
Barnesiella spp.	1.5E7		3.0E6 -2.9E8
Odoribacter spp.	3.1E6		<=9.5E7
Prevotella spp.	6.5E7 L		6.6E7 -3.8E9
Firmicutes Phylum			
Anaerotruncus colihominis/massiliensis	<DL		<=2.0E7
Butyrivibrio crossotus	<DL		<=3.3E7
Clostridium spp.	1.1E6		<=1.5E7
Coprococcus eutactus	1.1E6		<=1.2E8
Faecalibacterium prausnitzii	1.1E7		1.1E6 -1.1E9
Lactobacillus spp.	<DL		<=1.6E6
Pseudoflavonifractor spp.	1.2E6		1.3E4 -2.9E7
Roseburia spp.	5.3E6		3.6E5 -4.6E8
Ruminococcus bromii	7.6E7		<=1.5E9
Veillonella spp.	2.0E5		<=4.1E6
Actinobacteria Phylum			
Bifidobacterium spp.	6.0E6		4.6E5 -2.6E8
Bifidobacterium longum subsp. longum	8.1E4		<=1.3E8
Collinsella aerofaciens	1.4E6		<=1.3E8
Proteobacteria Phylum			
Desulfovibrio piger	<DL		<=5.4E7
Escherichia coli	4.3E5		<=7.5E6
Oxalobacter formigenes	2.5E4		<=1.1E7
Euryarchaeota Phylum			
Methanobrevibacter smithii	4.3E6		<=2.0E7
Fusobacteria Phylum			
Fusobacterium spp.	<DL		<=1.8E5
Verrucomicrobia Phylum			
Akkermansia muciniphila	1.1E6		>=8.5E3

GENOVA DIAGNOSTICS

Methodology: Culture/MALDI-TOF MS, Automated and Manual Bioc

Gastr

Human microflora is influenced by environmental fac
competitive ecosystem of the organisms in the GI tra
significance should be based upon clinical symptoms

Microbiology Legend

NG	NP	PP
No Growth	Non-Pathogen	Potential Pathogen

Bacteriology (Culture)

Lactobacillus spp.

Escherichia coli

Bifidobacterium (Anaerobic Culture)

Additional Bacteria

Salmonella spp.

Shigella spp.

alpha haemolytic Streptococcus

Mucoid Escherichia coli

Enterococcus hirae (Group D)

Bacillus species

Mycology (Culture)

Candida albicans

Geotrichum species

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 Additiona
reference of all

Genus/specie	
Nematodes -	
Ancylostoma/Ne	
Ascaris lumbricc	
Capillaria philip	
Enterobius verm	
Strongyloides st	
Trichuris trichiur	
Cestodes - ta	
Diphyllobothrium	
Dipylidium canir	
Hymenolepis dii	
Hymenolepis na	
Taenia spp.	
Trematodes	
Clonorchis/Opis	
Fasciola spp./ F	
Heterophyes/Me	
Paragonimus sp	
Schistosoma sp	
Protozoa	
Balantidium coli	
Blastocystis sp	
Chilomastix mes	
Cryptosporidium	
Cyclospora caye	
Dientamoeba fra	
Entamoeba coli	
Entamoeba hist	
Entamoeba hart	
Entamoeba pole	
Endolimax nana	
Giardia	Not Detected
Iodamoeba buetschlii	Not Detected
Cystoisospora spp.	Not Detected
Trichomonads (e.g. *Pentatrichomonas*)	Not Detected
Additional Findings	
White Blood Cells	Not Detected
Charcot-Leyden Crystals	Not Detected
Other Infectious Findings	

Parasitology

PCR Parasitology - Protozoa

Methodologies: DNA by PCR

Organism	Result	Units		Expected Result
Blastocystis spp.	<2.14e2	femtograms/microliter C&S stool	Not Detected	Not Detected
Cryptosporidium parvum/hominis	<1.76e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Cyclospora cayetanensis	<2.65e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Dientamoeba fragilis	2.32e2	genome copies/microliter C&S stool	Detected	Not Detected
Entamoeba histolytica	<9.64e1	genome copies/microliter C&S stool	Not Detected	Not Detected
Giardia	<1.36e1	genome copies/microliter C&S stool	Not Detected	Not Detected

Additional Results

Methodology: Fecal Immunochemical Testing (FIT)

	Result	Expected Value
Fecal Occult Blood♦	Negative	Negative
Color††	Brown	
Consistency††	Formed/Normal	

††Results provided from patient input.

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.

GENOVA DIAGNOSTICS

Case #3 – Summary and Next Steps

- High Scores in the Infection and Dysbiosis Functional Pillars
- Culture positive for two yeasts –
  - *Candida albicans*
  - *Geotrichum species*
- *Dientamoeba fragilis* O&P and qPCR

- Brain fog
- Fatigue
- Occasional diarrhea

- Yeast and *D. fragilis* - Now what?

GENOVA DIAGNOSTICS

Treatment - Yeast

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

Mycology Sensitivity

Candida Susceptibility Profile for Azoles*

Organism	Number of Isolates	% Sensitive	
		Fluconazole	Voriconazole
Candida albicans	25561	99.19%	99.51%
Candida parapsilosis	8777	98.64%	99.33%
Candida kruseii	3420	0.23%	97.7%
Candida tropicalis	1076	93.22%	90.5
Candida glabrata	2898	27.1%	90.

***Results of pharmaceutical sensitivities against certain yeast species are based on internal Genova dat specific yeast to the listed antifungal agent. The pharmaceutical results are not patient-specific. Conve agents are patient-specific.**

Non-absorbed Antifungals

Candida albicans	LOW INHIBITION
Nystatin	

Natural Agents

Candida albicans	LOW INHIBITION
Berberine	
Caprylic Acid	
Garlic	
Undecylenic Acid	
Uva-Ursi	

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

Mycology Sensitivity

Non-absorbed Antifungals

Geotrichum species	LOW INHIBITION	HIGH INHIBITION
Nystatin		

Natural Agents

Geotrichum species	LOW INHIBITION	HIGH INHIBITION
Berberine		
Caprylic Acid		
Garlic		
Undecylenic Acid		
Uva-Ursi		

GENOVA DIAGNOSTICS

Treatment Parasites

- Why don’t we provide sensitivities for parasites?
  - They’re not alive
- cdc.gov/parasites

Treatment

Examples of several of the most commonly used treatments are provided in the table below. As always, treatment decisions should be individualized.

Drug*	Dosage regimen for adults
Iodoquinol	650 mg orally three times daily for 20 days
OR	
Paromomycin	25–35 mg per kg per day orally, in three divided doses, for 7 days
OR	
Metronidazole**	500–750 mg orally three times daily for 10 days

Herbal therapeutics for parasites

- Not a ton of literature –
  - Mainly anecdotal
- Antimicrobial herbs have wide application beyond just bacteria (viruses, protozoa, worms)
- Lit dive PubMed/Google Scholar
- Supplement specialists!!
- Naturopathic database

- Usual suspects:
  - Black walnut
  - Artemesia/Wormwood
  - Oregano leaf/oil
  - Garlic
  - Berberine
  - Olive leaf extract

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9652050/
https://pubmed.ncbi.nlm.nih.gov/27867026/
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2758403/
https://parasitesandvectors.biomedcentral.com/articles/10.1186/s13071-015-0942-y
https://www.researchgate.net/profile/Fatima-Mohammad-Allebawi/publication/333968744

Case Study #4

- 64 yr. old male
- PMHx of long-standing OA
- NSAID and acetaminophen use
- No alcohol or tobacco

- “Can’t eat” – very limited diet
- Mid-epigastric pain
- Nausea
- No diarrhea/constipation

2200 GI Effects™ Comprehensive Pro

MALDIGESTION

INFECTION

Key (< 2 : Low Need for Support) (2-3 : Opti

	Need for Digestive Support	Need for Inflammation Mod
	MALDIGESTION	INFLAMMATIO
	5	4
Biomarkers	Pancreatic Elastase ▽ Products of Protein Breakdown ▽ Fecal Fats ▽	Calprotectin Eosinophil Protein X Secretory IgA Occult Blood
ic Support Options	• Digestive Enzymes • Betaine HCl • Bile Salts • Apple Cider Vinegar • Mindful Eating Habits • Digestive Bitters	• Elimination Diet/ Foc Sensitivity Testing • Mucosa Support: Sli Elm, Althea, Aloe, D • Zinc Carnosine • L-Glutamine • Quercetin

Commensal Abund

Patient Total Commens

Total Commensal Abundanc healthy cohort. Low levels of cc prebiotic-rich foods and may in potential bacteria overgrowth o

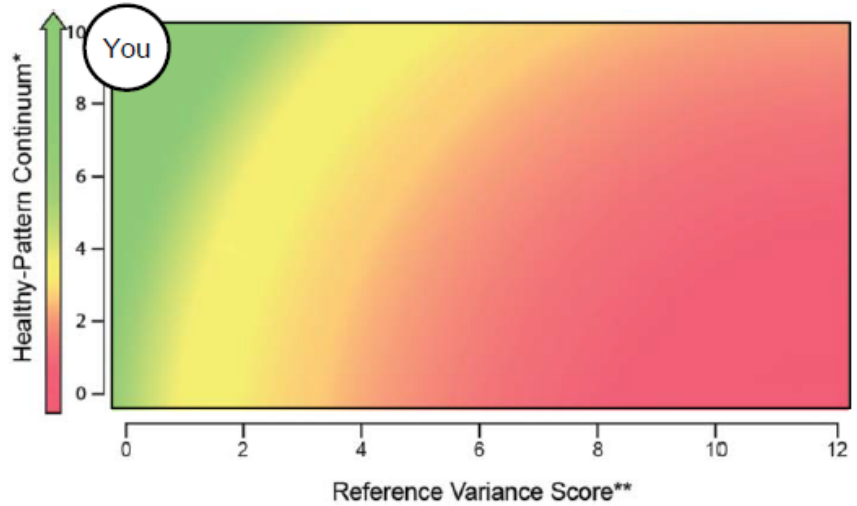
Dysbiosis Patterns

Inflammation-Associated D

Methane Dysbiosis Score

Commensal Microbiome Analysis

Commensal Balance

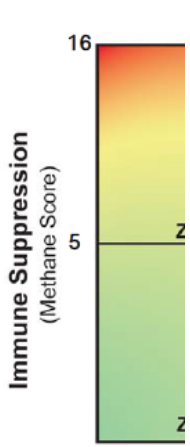


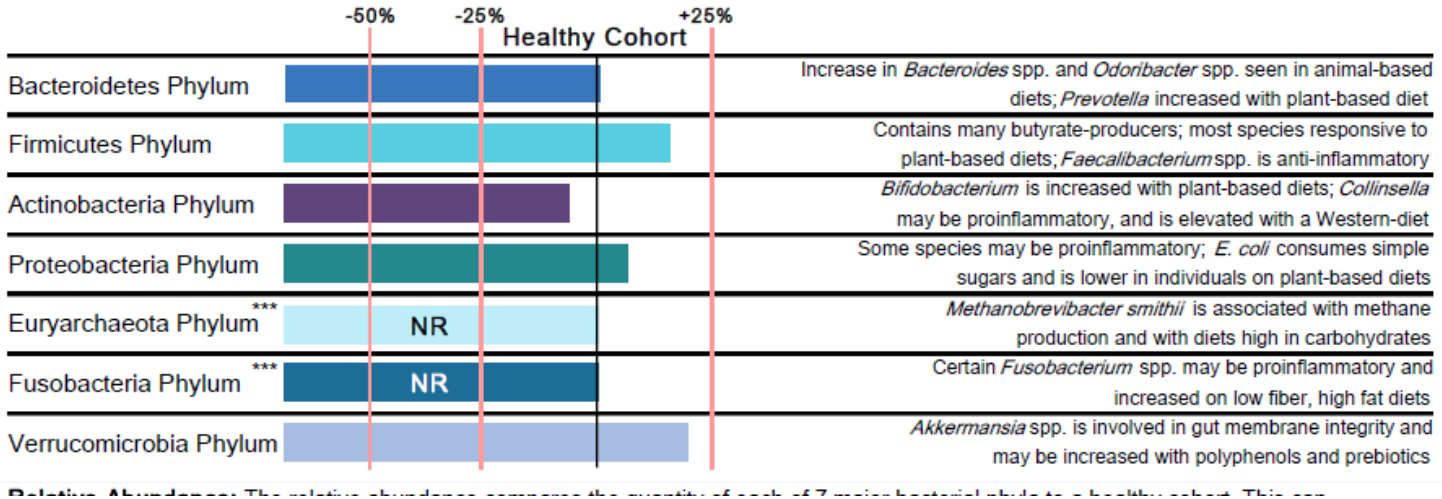
Balanced	Represents 95% of healthy individuals
Borderline	Represents 5% of healthy individuals
Imbalanced	Represents 60% of unhealthy individuals

*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.

**The total number of commensal bacteria (qPCR) that are out of balance for this individual on a scale of 0 to >12.

Relative Commensal Abundance





Bacteroidetes Phylum	Increase in *Bacteroides* spp. and *Odoribacter* spp. seen in animal-based diets; *Prevotella* increased with plant-based diet
Firmicutes Phylum	Contains many butyrate-producers; most species responsive to plant-based diets; *Faecalibacterium* spp. is anti-inflammatory
Actinobacteria Phylum	*Bifidobacterium* is increased with plant-based diets; *Collinsella* may be proinflammatory, and is elevated with a Western-diet
Proteobacteria Phylum	Some species may be proinflammatory; *E. coli* consumes simple sugars and is lower in individuals on plant-based diets
Euryarchaeota Phylum*** NR	*Methanobrevibacter smithii* is associated with methane production and with diets high in carbohydrates
Fusobacteria Phylum*** NR	Certain *Fusobacterium* spp. may be proinflammatory and increased on low fiber, high fat diets
Verrucomicrobia Phylum	*Akkermansia* spp. is involved in gut membrane integrity and may be increased with polyphenols and prebiotics

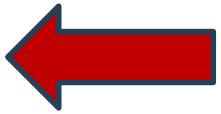
Relative Abundance: The relative abundance compares the quantity of each of 7 major bacterial phyla to a healthy cohort. This can

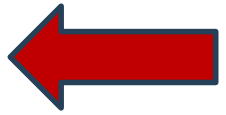
GENOVA DIAGNOSTICS

2200 GI Effects™ Comprehensive Profile - Stool

Methodology: GC-FID, Automated Chemistry, EIA

	Result	QUINTILE DISTRIBUTION (1st 2nd 3rd 4th 5th)	Reference Range
Digestion and Absorption			
Pancreatic Elastase 1 †	155 L	100 200	>200 mcg/g
Products of Protein Breakdown (Total*) (Valerate, Isobutyrate, Isovalerate)	1.7 L		1.8-9.9 micromol/g
Fecal Fat (Total*)	4.4		3.2-38.6 mg/g
Triglycerides	0.4		0.3-2.8 mg/g
Long-Chain Fatty Acids	2.6		1.2-29.1 mg/g
Cholesterol	0.4		0.4-4.8 mg/g
Phospholipids	1.0		0.2-6.9 mg/g
Inflammation and Immunology			
Calprotectin †	64 H	50 120	<=50 mcg/g
Eosinophil Protein X (EPX)†	<DL	0.5 2.7	<=2.7 mcg/g
Fecal secretory IgA	<150	680 2040	<=2,040 mcg/mL
Gut Microbiome Metabolites			
Metabolic			
Short-Chain Fatty Acids (SCFA) (Total*) (Acetate, n-Butyrate, Propionate)	17.7 L		>=23.3 micromol/g
n-Butyrate Concentration	3.4 L		>=3.6 micromol/g
n-Butyrate %	19.2		11.8-33.3 %
Acetate %	57.6		48.1-69.2 %
Propionate %	23.0		<=29.3 %
Beta-glucuronidase	3,125		368-6,266 U/g





GENOVA DIAGNOSTICS

Gastrointestinal Microbiome (PCR)

Commensal Bacteria (PCR)

Result CFU/g stool | QUINTILE DISTRIBUTION 1st 2nd 3rd 4th 5th | Reference Range CFU/g stool

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

Bacteroidetes Phylum
- *Bacteroides uniformis*
- *Phocaeicola vulgatus*
- *Barnesiella spp.*
- *Odoribacter spp.*
- *Prevotella spp.*

Firmicutes Phylum
- *Anaerotruncus colihon*
- *Butyrivibrio crossotus*
- *Clostridium spp.*
- *Coprococcus eutactus*
- *Faecalibacterium prau*
- *Lactobacillus spp.*
- *Pseudoflavonifractor s*
- *Roseburia spp.*
- *Ruminococcus bromii*
- *Veillonella spp.*

Actinobacteria Phylum
- *Bifidobacterium spp.*
- *Bifidobacterium l*
- *Collinsella aerofaciens*

Proteobacteria Phylum
- *Desulfovibrio piger*
- *Escherichia coli*
- *Oxalobacter formigene*

Euryarchaeota Phylum
- *Methanobrevibacter s*

Fusobacteria Phylum
- *Fusobacterium spp.*

Verrucomicrobia Phyl
- *Akkermansia muciniph*

Gastrointestinal Microbiome (Culture)

Human microflora is influenced by environmental factors and the competitive ecosystem of the o significance should be based u

Microbic

NG	NP
No Growth	Non-Pathogen

Bacteriology (Culture

Lactobacillus spp.

Escherichia coli

Bifidobacterium (Anaerobic Culture

Additional Bacteria

Salmonella spp.

Shigella spp.

alpha haemolytic Streptococcus

Enterococcus faecalis

Proteus mirabilis

Enterobacter cloacae

Mycology (Culture)

Yeast, not Candida albicans

Additional Bacteria

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. These results were obtained using wet preparation(s) and trichrome stained smear. For an extensive reference of all potentially detectable organisms, please visit www.gdx.net/product/gi-effects-comprehensive-stool-test

Genus/species	Result
Nematodes - roundworr	
Ancylostoma/Necator (Hookv	
Ascaris lumbricoides	
Capillaria philippinensis	
Enterobius vermicularis	
Strongyloides stercoralis	
Trichuris trichiura	
Cestodes - tapeworms	
Diphyllobothrium latum	
Dipylidium caninum	
Hymenolepis diminuta	
Hymenolepis nana	
Taenia spp.	
Trematodes - flukes	
Clonorchis/Opisthorchis spp.	
Fasciola spp./ *Fasciolopsis b*	
Heterophyes/Metagonimus	
Paragonimus spp.	
Schistosoma spp.	
Protozoa	
Balantidium coli	
Blastocystis spp.	
Chilomastix mesnili	
Cryptosporidium spp.	
Cyclospora cayetanensis	
Dientamoeba fragilis	
Entamoeba coli	
Entamoeba histolytica/dispar	
Entamoeba hartmanii	
Entamoeba polecki	
Endolimax nana	
Giardia	
Iodamoeba buetschlii	
Cystoisospora spp.	
Trichomonads (e.g. *Pentatrichomonas*)	Not Detected
Additional Findings	
White Blood Cells	Not Detected
Charcot-Leyden Crystals	Not Detected
Other Infectious Findings	

Parasitology

PCR Parasitology - Protozoa

Methodologies: DNA by PCR

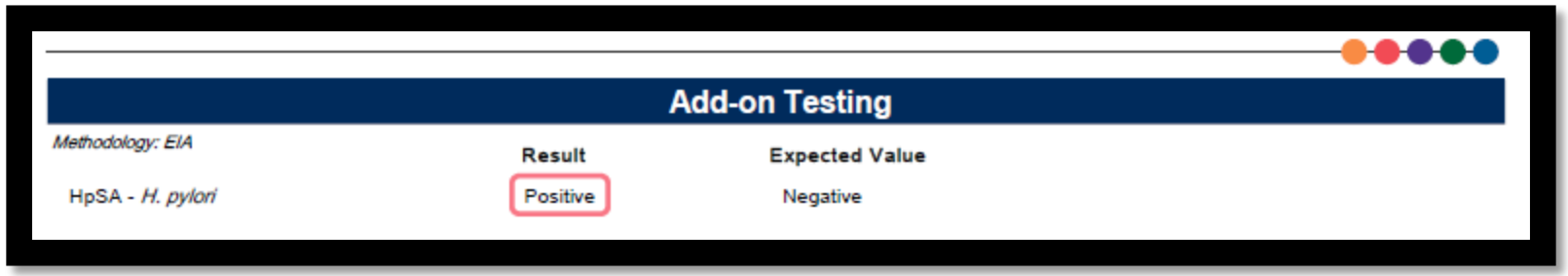
Organism	Result	Units		Expected Result
Blastocystis spp.	<2.14e2	femtograms/microliter C&S stool	Not Detected	Not Detected
Cryptosporidium parvum/hominis	<1.76e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Cyclospora cayetanensis	<2.65e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Dientamoeba fragilis	<1.84e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Entamoeba histolytica	<9.64e1	genome copies/microliter C&S stool	Not Detected	Not Detected
Giardia	<1.36e1	genome copies/microliter C&S stool	Not Detected	Not Detected

Additional Results

Methodology: Fecal Immunochemical Testing (FIT)

	Result	Expected Value
Fecal Occult Blood✦	Negative	Negative
Color††	Not Given	
Consistency††	Not Given	

GENOVA DIAGNOSTICS



Add-on Testing

Methodology: EIA

	Result	Expected Value
HpSA - *H. pylori*	Positive	Negative

GENOVA DIAGNOSTICS

Helicobacter pylori – Add-on

- ACG does not recommend wide-spread screening
- Urea breath testing, stool surface antigen, endoscopy/biopsy
- ACG Indications for add-on:

Table 1. Indications for Diagnosis and Treatment of *H. pylori*

Established
- Active peptic ulcer disease (gastric or duodenal ulcer)
- Confirmed history of peptic ulcer disease (not previously treated for *H. pylori*)
- Gastric MALT lymphoma (low grade)
- After endoscopic resection of early gastric cancer
- Uninvestigated dyspepsia (depending upon *H. pylori* prevalence)

Controversial
- Nonulcer dyspepsia
- Gastroesophageal reflux disease
- Persons using nonsteroidal antiinflammatory drugs
- Unexplained iron deficiency anemia
- Populations at higher risk for gastric cancer

GENOVA DIAGNOSTICS

https://journals.lww.com/ajg/fulltext/2017/02000/acg_clinical_guideline__treatment_of_helicobacter.12.aspx

Case Study #4 – Summary and Next Steps

- Every Functional Pillar with some need (Yellow)
- Markers of Digestion/Absorption all low
- Mid-grade inflammation – Calprotectin of 64
- Low SCFA's
- 2 Potential Pathogens in culture
- Positive H. pylori surface antigen

- Mid-epigastric pain – "can't eat"
- Nausea
- No diarrhea or constipation

GENOVA DIAGNOSTICS

Things to consider……..

- 2 Potential Pathogens in culture but no diarrhea
  - Need to treat?
  - Support with pre- and probiotics given limited diet
  - If treating *H. pylori* with antimicrobials - would likely cover
- Mid-grade inflammation (Calprotectin)
  - Is it all from *H. pylori*?
  - 64 years old – need for colonoscopy – review to ensure cancer screenings up to date!
- Treating *H. pylori*
  - Prescriptive agents
  - Herbal therapeutics
  - Need for endoscopy given severity of symptoms?

Treatment

Regimen	Drugs (doses)	Dosing frequency	Duration (days)	FDA approval
Clarithromycin triple	PPI (standard or double dose)	BID	14	Yes[a]
	Clarithromycin (500 mg)			
	Amoxicillin (1 grm) or Metronidazole (500 mg TID)			
Bismuth quadruple	PPI (standard dose)	BID	10–14	No[b]
	Bismuth subcitrate (120–300 mg) or subsalicylate (300 mg)	QID		
	Tetracycline (500 mg)	QID		
	Metronidazole (250–500 mg)	QID (250)		
		TID to QID (500)		
Concomitant	PPI (standard dose)	BID	10–14	No
	Clarithromycin (500 mg)			
	Amoxicillin (1 grm)			
	Nitroimidazole (500 mg)[c]			
Sequential	PPI (standard dose)+Amoxicillin (1 grm)	BID	5–7	No
	PPI, Clarithromycin (500 mg)+Nitroimidazole (500 mg)[c]	BID	5–7	
Hybrid	PPI (standard dose)+Amox (1 grm)	BID	7	No
	PPI, Amox, Clarithromycin (500 mg), Nitroimidazole (500 mg)[c]	BID	7	
Levofloxacin triple	PPI (standard dose)	BID	10–14	No
	Levofloxacin (500 mg)	QD		
	Amox (1 grm)	BID		
Levofloxacin sequential	PPI (standard or double dose)+Amox (1 grm)	BID	5–7	No
	PPI, Amox, Levofloxacin (500 mg QD), Nitroimidazole (500 mg)[c]	BID	5–7	
LOAD	Levofloxacin (250 mg)	QD	7–10	No
	PPI (double dose)	QD		
	Nitazoxanide (500 mg)	BID		
	Doxycycline (100 mg)	QD		

BID, twice daily; FDA, Food and Drug Administration; PPI, proton pump inhibitor; TID, three times daily; QD, once daily; QID, four times daily.

[a]Several PPI, clarithromycin, and amoxicillin combinations have achieved FDA approval. PPI, clarithromycin and metronidazole is not an FDA-approved treatment regimen.

[b]PPI, bismuth, tetracycline, and metronidazole prescribed separately is not an FDA-approved treatment regimen. However, Pylera, a combination product containing bismuth subcitrate, tetracycline, and metronidazole combined with a PPI for 10 days is an FDA-approved treatment regimen.

[c]Metronidazole or tinidazole.

GENOVA DIAGNOSTICS

https://journals.lww.com/ajg/fulltext/2017/02000/acg_clinical_guideline__treatment_of_helicobacter.12.aspx

Herbal Therapeutics

- Mastic gum
- Zinc carnosine
- Berberine
- Bismuth Citrate
- Curcumin
- Ginger
- Propolis

http://www.ncbi.nlm.nih.gov/pubmed/19879118
http://gut.bmj.com/content/56/2/168.abstract
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4848239/
https://www.tandfonline.com/doi/abs/10.1080/1040841X.2021.1975643
Zhang, D.; Ke, L.; Ni, Z.; Chen, Y.; Zhang, L.-H.; Zhu, S.-H.; Li, C.-J.; Shang, L.; Liang, J.; Shi, Y.-Q.. Medicine 2017, 96

Case Study #5

- 38 yr. old male
- No PMHx, no meds
- Weekend warrior athlete
- Biohacker – into wellness taking many supplements

- No physical complaints
- Looking to optimize health given family history of premature heart disease and colon cancer

GENOVA DIAGNOSTICS

2200 GI Effects™ Comprehensive Profile -

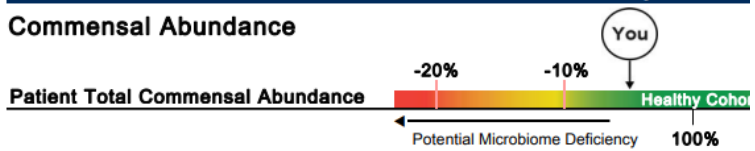
Fur

Key (< 2 : Low Need for Support (2-3 : Optional N

	Need for Digestive Support	Need for Inflammation Modulatio
	MALDIGESTION	INFLAMMATION
	0	0
Biomarkers	Fecal Fats ▽ Pancreatic Elastase ● Products of Protein Breakdown ●	Calprotectin Eosinophil Protein X Secretory IgA Occult Blood
Therapeutic Support Options	• Digestive Enzymes • Betaine HCl • Bile Salts • Apple Cider Vinegar • Mindful Eating Habits • Digestive Bitters	• Elimination Diet/ Food Sensitivity Testing • Mucosa Support: Slippery Elm, Althea, Aloe, DGL, e • Zinc Carnosine • L-Glutamine • Quercetin • Turmeric • Omega-3's • GI Referral (If Calpro is Elevated)

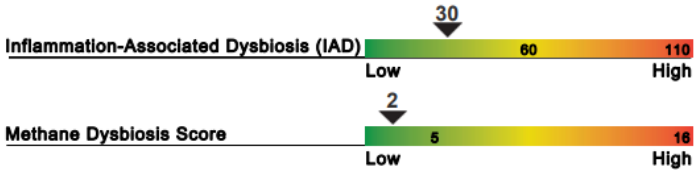
Commensal Microbiome Analysis

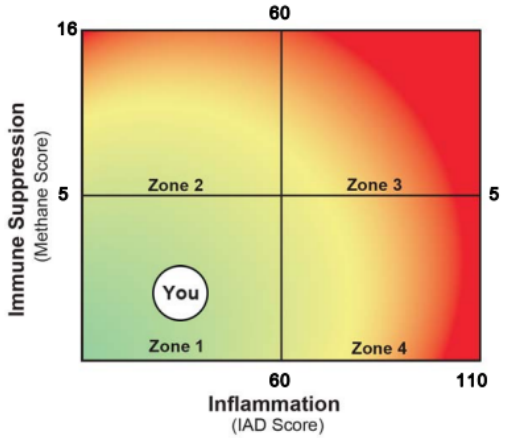
Commensal Abundance



Total Commensal Abundance: The total commensal abundance is a sum-total of the reported comm healthy cohort. Low levels of commensal bacteria are often observed after antimicrobial therapy, or in die prebiotic-rich foods and may indicate the need for microbiome support. Conversely, higher total commen potential bacteria overgrowth or probiotic supplementation.

Dysbiosis Patterns





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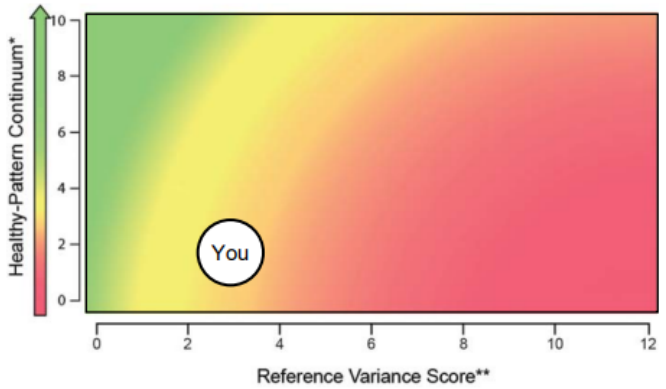
Commensal Microbiome Analysis

Commensal Balance

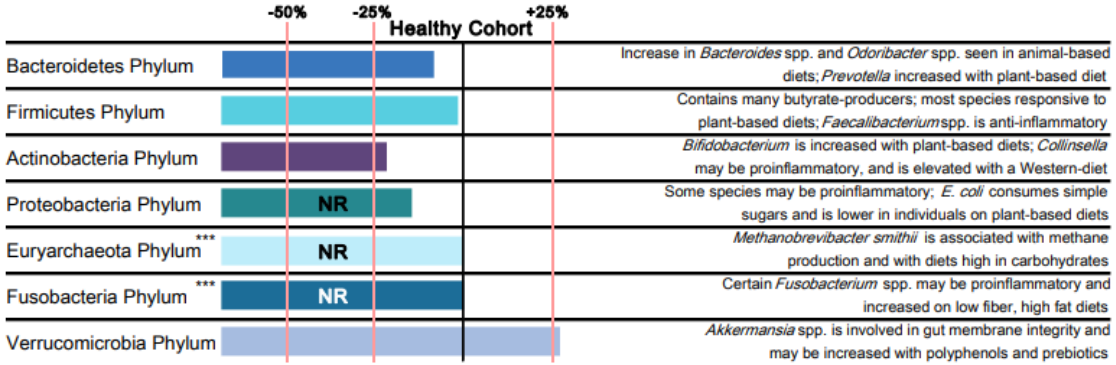


Balanced	Represents 95% of healthy individuals
Borderline	Represents 5% of healthy individuals
Imbalanced	Represents 60% of unhealthy individuals

*A progressive ranking scale based on a Genova proprietary algorithm that differentiates healthy and unhealthy commensal patterns.

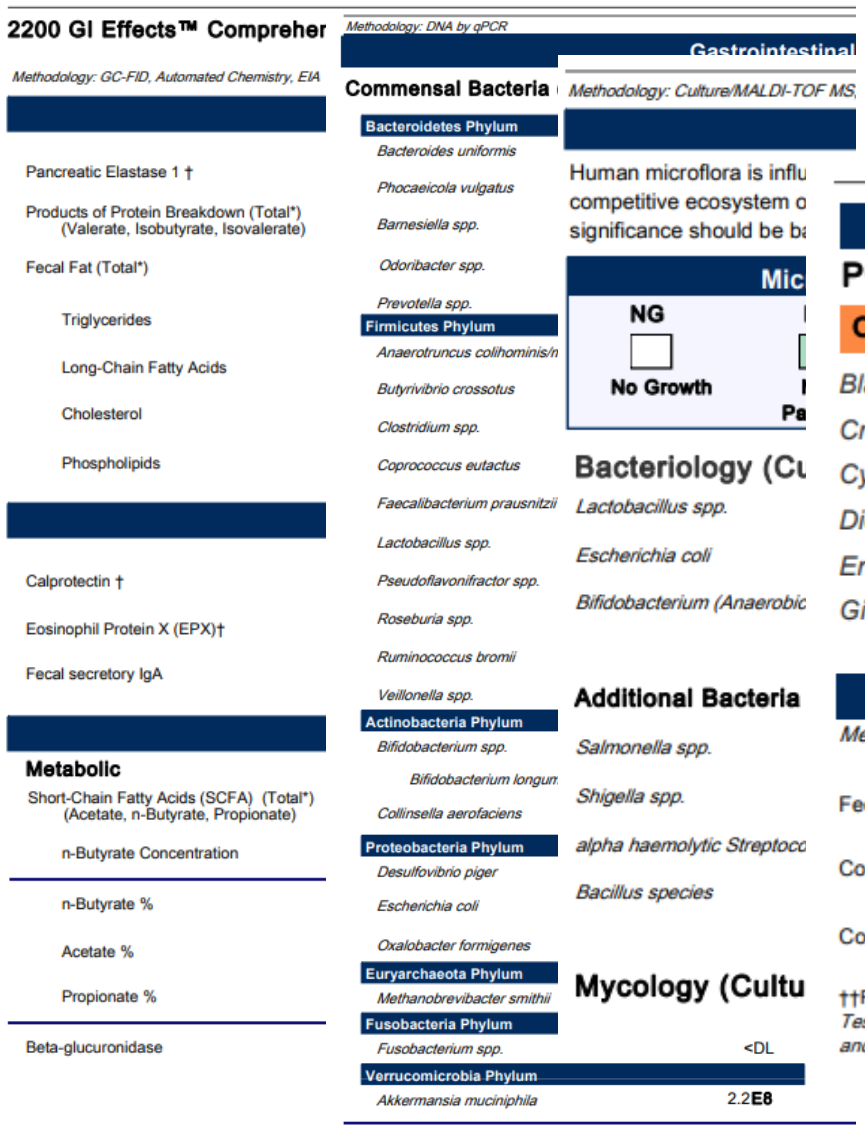
**The total number of commensal bacteria (qPCR) that are out of balance for this individual on a scale of 0 to >12.

Relative Commensal Abundance



Relative Abundance: The relative abundance compares the quantity of each of 7 major bacterial phyla to a healthy cohort. This can indicate broader variances in the patient's gut microbiome profile. Certain interventions may promote or limit individual phyla when clinically appropriate. Please refer to Genova's Stool Testing Support Guide for more information on modulation of commensal bacteria through diet & nutrient interventions. ***Approximately 70% of the healthy cohort had below detectable levels of *Methanobrevibacter smithii*. Approximately 90% of the healthy cohort had below detectable levels of *Fusobacterium spp.*

GENOVA DIAGNOSTICS



2200 GI Effects™ Compreher

Methodology: GC-FID, Automated Chemistry, EIA

Pancreatic Elastase 1 †

Products of Protein Breakdown (Total*)
(Valerate, Isobutyrate, Isovalerate)

Fecal Fat (Total*)

Triglycerides

Long-Chain Fatty Acids

Cholesterol

Phospholipids

Calprotectin †

Eosinophil Protein X (EPX)†

Fecal secretory IgA

Metabolic

Short-Chain Fatty Acids (SCFA) (Total*)
(Acetate, n-Butyrate, Propionate)

n-Butyrate Concentration

n-Butyrate %

Acetate %

Propionate %

Beta-glucuronidase

Methodology: DNA by qPCR

Gastrointestinal

Commensal Bacteria

Bacteroidetes Phylum

Bacteroides uniformis

Phocaeicola vulgatus

Barnesiella spp.

Odoribacter spp.

Prevotella spp.

Firmicutes Phylum

Anaerotruncus colihominis/n

Butyrivibrio crossotus

Clostridium spp.

Coprococcus eutactus

Faecalibacterium prausnitzii

Lactobacillus spp.

Pseudoflavonifractor spp.

Roseburia spp.

Ruminococcus bromii

Veillonella spp.

Actinobacteria Phylum

Bifidobacterium spp.

Bifidobacterium longum

Collinsella aerofaciens

Proteobacteria Phylum

Desulfovibrio piger

Escherichia coli

Oxalobacter formigenes

Euryarchaeota Phylum

Methanobrevibacter smithii

Fusobacteria Phylum

Fusobacterium spp. <DL

Verrucomicrobia Phylum

Akkermansia muciniphila 2.2E8

Methodology: Culture/MALDI-TOF MS

Human microflora is influ
competitive ecosystem o
significance should be ba

Mic

NG

No Growth

Pa

Bacteriology (Cu

Lactobacillus spp.

Escherichia coli

Bifidobacterium (Anaerobic

Additional Bacteria

Salmonella spp.

Shigella spp.

alpha haemolytic Streptocc

Bacillus species

Mycology (Cultu

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. These results were obtained using wet preparation(s) and trichrome stained smear. For an extensive

Parasitology

PCR Parasitology - Protozoa

Methodologies: DNA by PCR

Organism	Result	Units		Expected Result
Blastocystis spp.	<2.14e2	femtograms/microliter C&S stool	Not Detected	Not Detected
Cryptosporidium parvum/hominis	<1.76e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Cyclospora cayetanensis	<2.65e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Dientamoeba fragilis	<1.84e2	genome copies/microliter C&S stool	Not Detected	Not Detected
Entamoeba histolytica	<9.64e1	genome copies/microliter C&S stool	Not Detected	Not Detected
Giardia	<1.36e1	genome copies/microliter C&S stool	Not Detected	Not Detected

Additional Results

Methodology: Fecal Immunochemical Testing (FIT)

	Result	Expected Value
Fecal Occult Blood◆	Negative	Negative
Color††	Black	
Consistency††	Formed/Normal	

††Results provided from patient input.

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.

GENOVA DIAGNOSTICS

Case Study #5 – Summary and Next Steps

- Unremarkable GI Effects Stool Profile

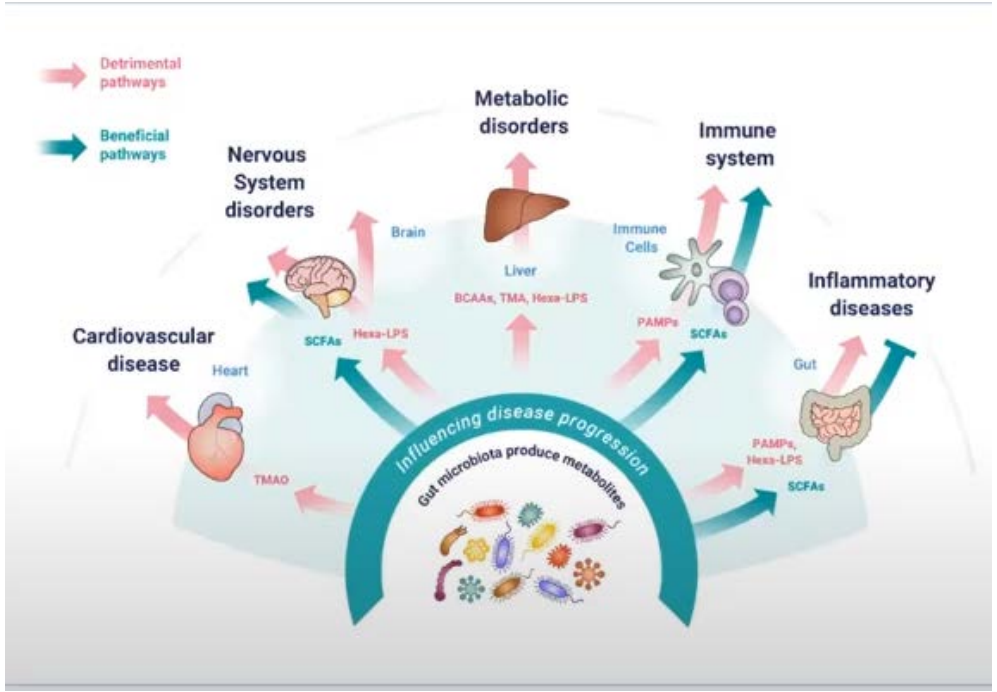
- No physical complaints
- Looking to optimize health

- The Microbiomix Profile
  - Digging even deeper!

GENOVA DIAGNOSTICS

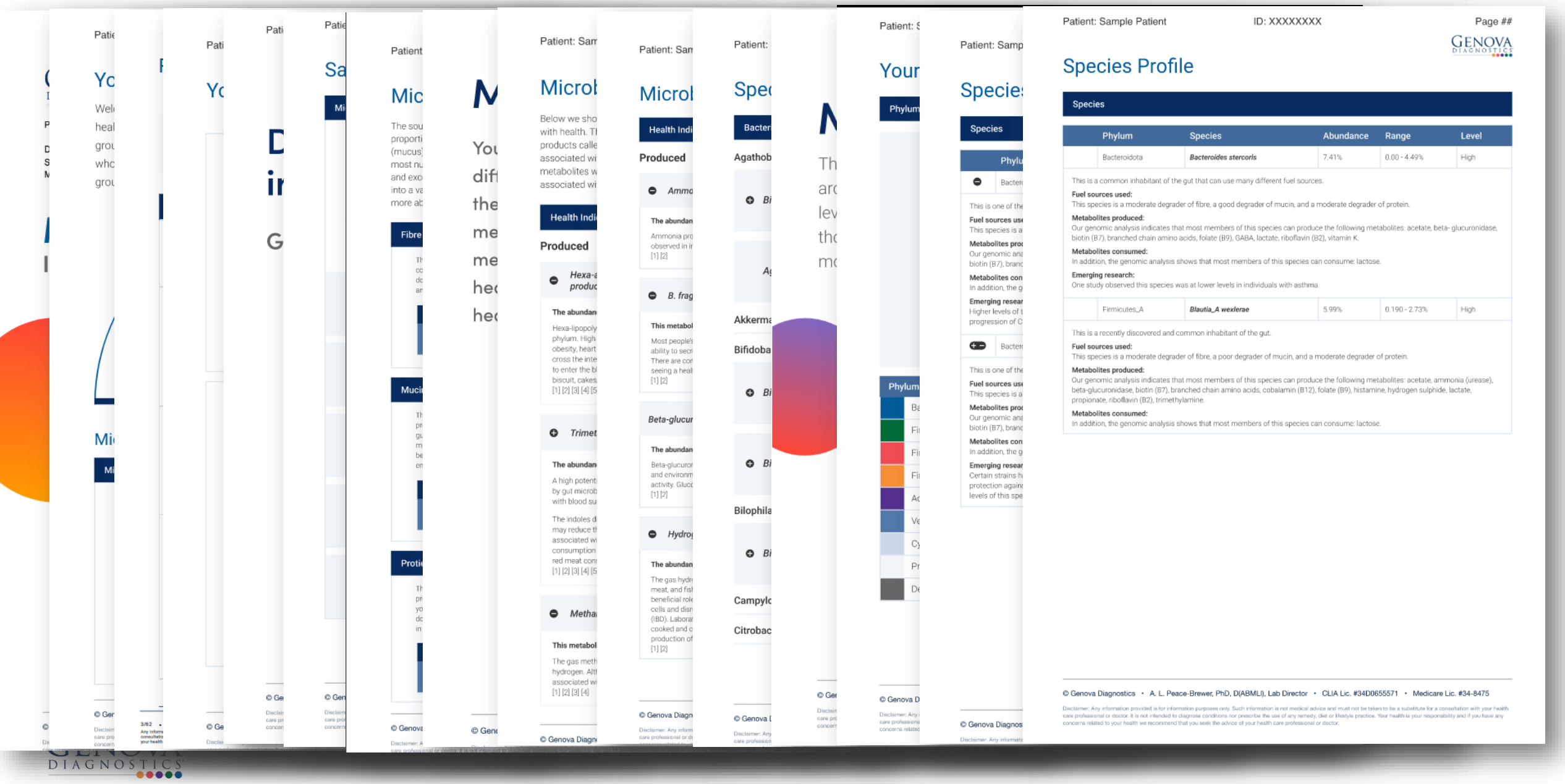
Microbiomix

Whole Genome Sequencing



- List of every species
- Potential to make metabolites
- Report Summary
- Shannon Diversity Index
- Literature cited education throughout the report
- Key Insights
- Species of Interest

GENOVA DIAGNOSTICS


Patient: Sample Patient
ID: XXXXXXXX
Page ##
GENOVA DIAGNOSTICS
Species Profile
Species
Phylum
Species
Abundance
Range
Level
Bacteroidota
Bacteroides stercoris
7.41%
0.00 - 4.49%
High
This is a common inhabitant of the gut that can use many different fuel sources.
Fuel sources used:
This species is a moderate degrader of fibre, a good degrader of mucin, and a moderate degrader of protein.
Metabolites produced:
Our genomic analysis indicates that most members of this species can produce the following metabolites: acetate, beta- glucuronidase, biotin (B7), branched chain amino acids, folate (B9), GABA, lactate, riboflavin (B2), vitamin K.
Metabolites consumed:
In addition, the genomic analysis shows that most members of this species can consume: lactose.
Emerging research:
One study observed this species was at lower levels in individuals with asthma.
Firmicutes_A
Blautia_A wexlerae
5.99%
0.190 - 2.73%
High
This is a recently discovered and common inhabitant of the gut.
Fuel sources used:
This species is a moderate degrader of fibre, a poor degrader of mucin, and a moderate degrader of protein.
Metabolites produced:
Our genomic analysis indicates that most members of this species can produce the following metabolites: acetate, ammonia (urease), beta-glucuronidase, biotin (B7), branched chain amino acids, cobalamin (B12), folate (B9), histamine, hydrogen sulphide, lactate, propionate, riboflavin (B2), trimethylamine.
Metabolites consumed:
In addition, the genomic analysis shows that most members of this species can consume: lactose.
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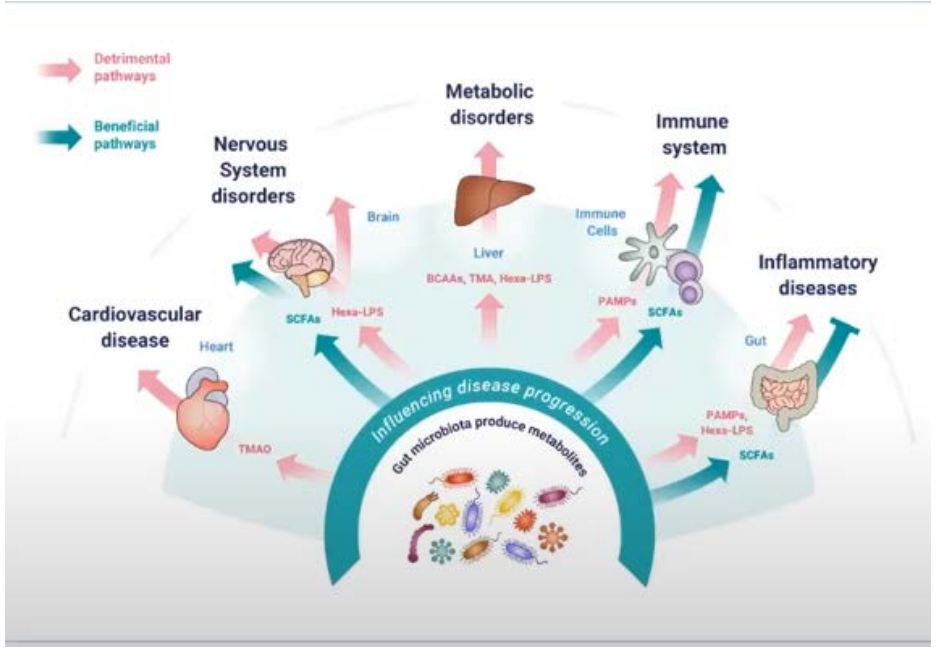
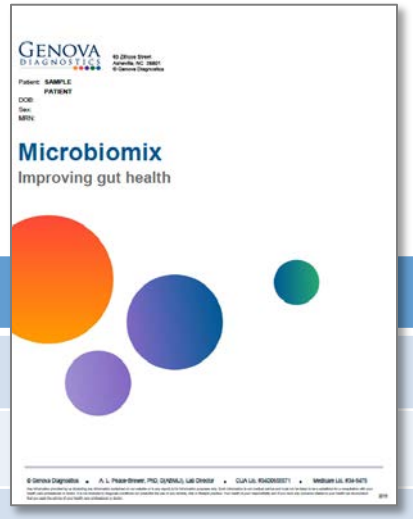
Refining Dysbiosis

- The real importance of “dysbiosis” may not be who is present or absent…
- It’s about what postbiotics (metabolites) are being created!
- This is why whole-genome sequencing will become invaluable in helping us understand the *functional* role of the microbiome
  - As compared to an attendance roll-call



Metabolites Assessed in Genova's *Microbiomix*



Metabolite	Clinical Considerations
Hexa-LPS	Contributor to inflammation
Trimethylamine	Cardiovascular risk factor (TMAO)
Methane & Hydrogen Sulfide Gas	Consideration for SIBO testing
Ammonia (Urease)	Protein recycling and risk for IP; consider Lactulose/Mannitol testing
B. fragilis toxin	Potential for infectious diarrhea
Beta-glucuronidase	Potential for excessive recirculation of toxins & steroid hormones
Oxalate consumption	Association with calcium oxalate kidney stones; consider additional testing
Neurotransmitters (GABA, IPA, Histamine)	Additional insight into gut-brain axis
SCFAs	Important for health of colonocytes
Vitamin production	Potential for GI synthesis of nutrients; consider NutrEval/Metabolomix

Case Study #5

- 38 yr. old male
- No PMHx, no meds
- Weekend warrior athlete
- Biohacker – into wellness taking many supplements

- No physical complaints
- Looking to optimize health given family history of premature heart disease and colon cancer

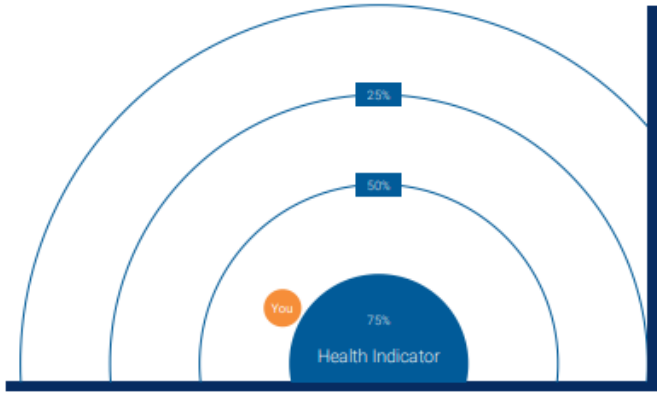
GENOVA DIAGNOSTICS

Microbiomix

Improving gut health

Your report overview

Welcome to the start of your journey to understanding how your microbiome affects your health. Throughout this report, the analyzed sample is compared to a healthy comparison group. This group is a collection of gut microbiome samples from everyday healthy people, who have not reported any significant health issues or symptoms. It represents a range of age groups, genders and diets.

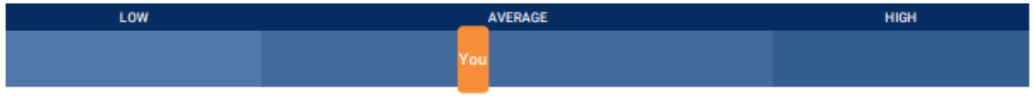


Your gut microbiome score is 69%. This measurement is an indication of how well your gut microbiome might be interacting with your overall health. A higher score suggests a more positive interaction.

Microbial Diversity

MICROBIAL DIVERSITY

Microbial diversity is a measure of the number of different microorganisms and the amount of each of these microorganisms in your sample. Average to high microbial diversity is associated with good health. A varied diet rich in plant-based foods such as fruits, vegetables, whole grains and nuts can help increase microbiome diversity. The Shannon Index is a measure of diversity which is used by members of the scientific community to compare results through time.



Your diversity level is
Average

Shannon Index
3.79

GENOVA DIAGNOSTICS

Report Summary

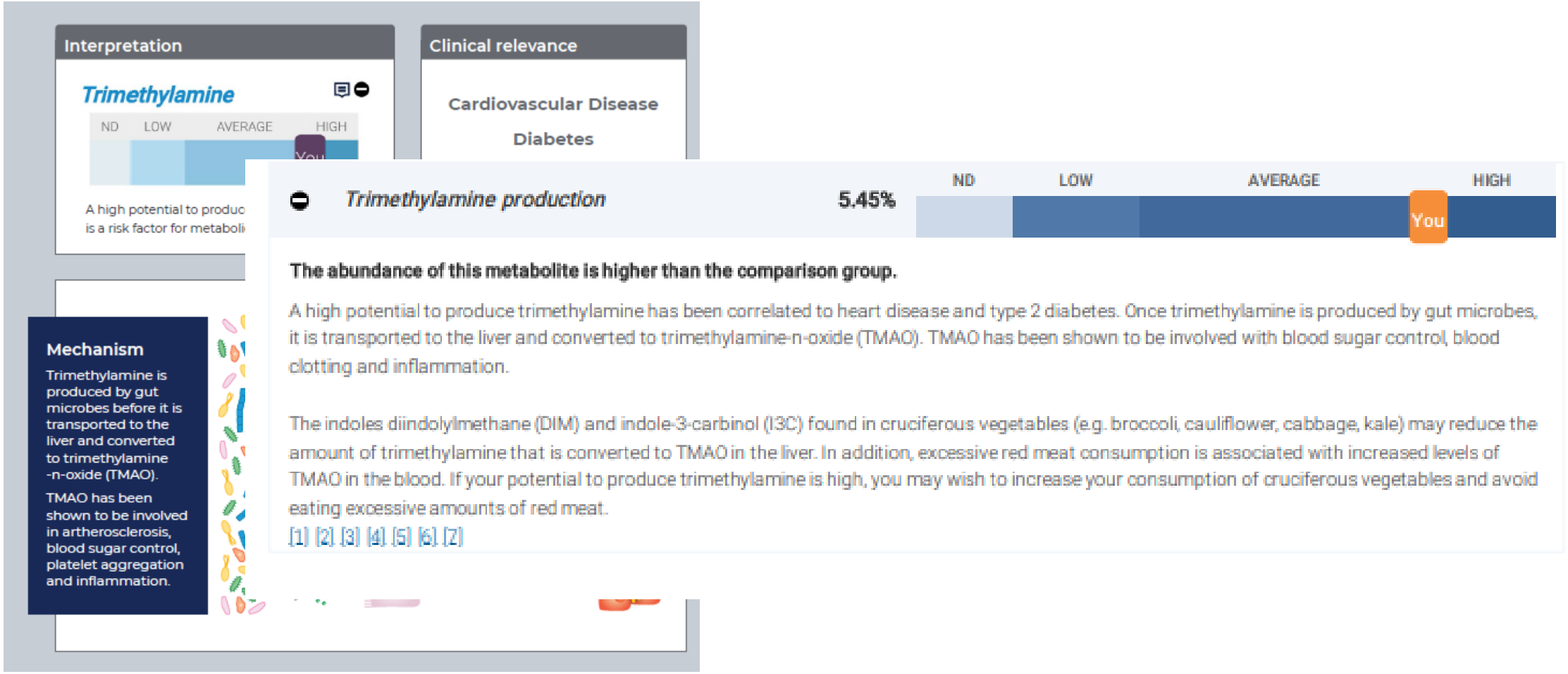
Sample ID: AD84B16A

Disclaimer: This report summary is provided to assist healthcare practitioners to interpret the Microbiomix report. The report should be used only after the health practitioner (you) has conducted a full client assessment which should include existing medications, allergies & intolerances and full client medical history.

Marker	Suggestion
Trimethylamine production (High)	**Increase Broccoli & Cauliflower, reduced meats** Trimethylamine (TMA) is a compound that can be produced by the microbiome which is converted to trimethylamine oxide (TMAO) in the liver, and has been correlated with heart disease and type 2 diabetes. The indoles diindolylmethane (DIM) and indole-3-carbinol (I3C) found in cruciferous vegetables (e.g. broccoli, cauliflower, cabbage, kale) may reduce the amount of trimethylamine that is converted to TMAO in the liver. In addition, excessive red meat consumption is associated with increased levels of TMAO in the blood. If your potential to produce trimethylamine is high, you may wish to increase your consumption of cruciferous vegetables and avoid eating excessive amounts of red meat. References [1] [2] [3] [4] [5] [6]
Hydrogen sulfide production (High)	**RS & FOS** Hydrogen sulfide is a gas that some intestinal bacteria produce by breaking down sulfur-containing amino acids. Elevated levels of hydrogen sulfide can inhibit energy production in intestinal cells as well as alter the mucus barrier of the intestine, and this has been associated with inflammatory bowel disease. To prevent elevated production of hydrogen sulfide, ensure intake of the amino acids methionine and cysteine is not excessive. Laboratory based studies have suggested that eating foods high in resistant starch (e.g. lentils, peas, beans, rolled oats and cooked and cooled potatoes) or Fructooligosaccharides (FOS) (e.g. onions, garlic, leek, banana, peaches, wheat, barley) can reduce the production of hydrogen sulfide by the microbiome. References [1] [2]

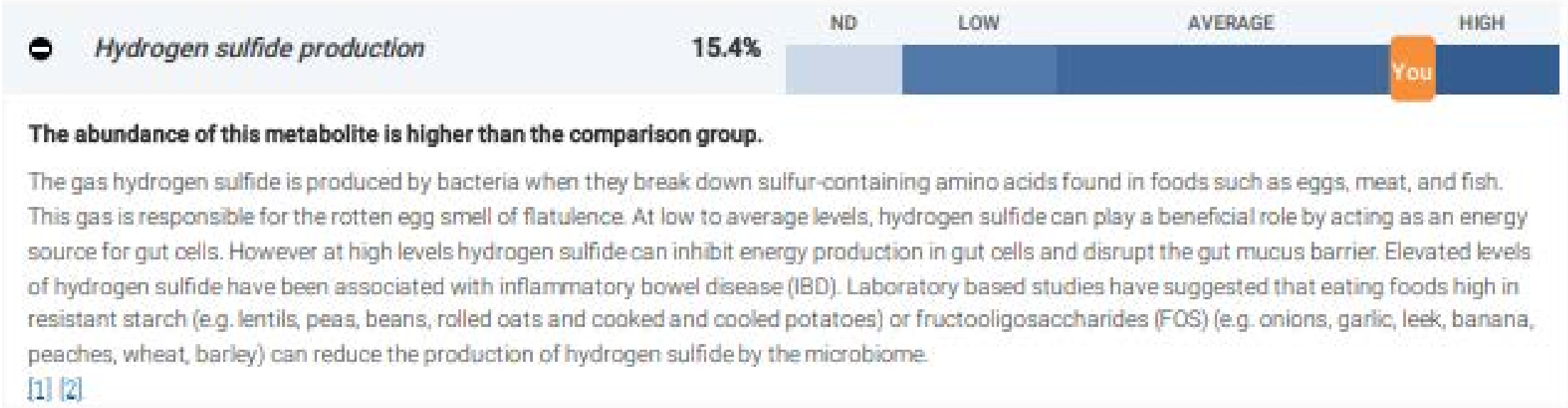
GENOVA DIAGNOSTICS

Trimethylamine (TMA)



GENOVA DIAGNOSTICS

Hydrogen sulfide



The abundance of this metabolite is higher than the comparison group.

The gas hydrogen sulfide is produced by bacteria when they break down sulfur-containing amino acids found in foods such as eggs, meat, and fish. This gas is responsible for the rotten egg smell of flatulence. At low to average levels, hydrogen sulfide can play a beneficial role by acting as an energy source for gut cells. However at high levels hydrogen sulfide can inhibit energy production in gut cells and disrupt the gut mucus barrier. Elevated levels of hydrogen sulfide have been associated with inflammatory bowel disease (IBD). Laboratory based studies have suggested that eating foods high in resistant starch (e.g. lentils, peas, beans, rolled oats and cooked and cooled potatoes) or fructooligosaccharides (FOS) (e.g. onions, garlic, leek, banana, peaches, wheat, barley) can reduce the production of hydrogen sulfide by the microbiome.

[1] [2]

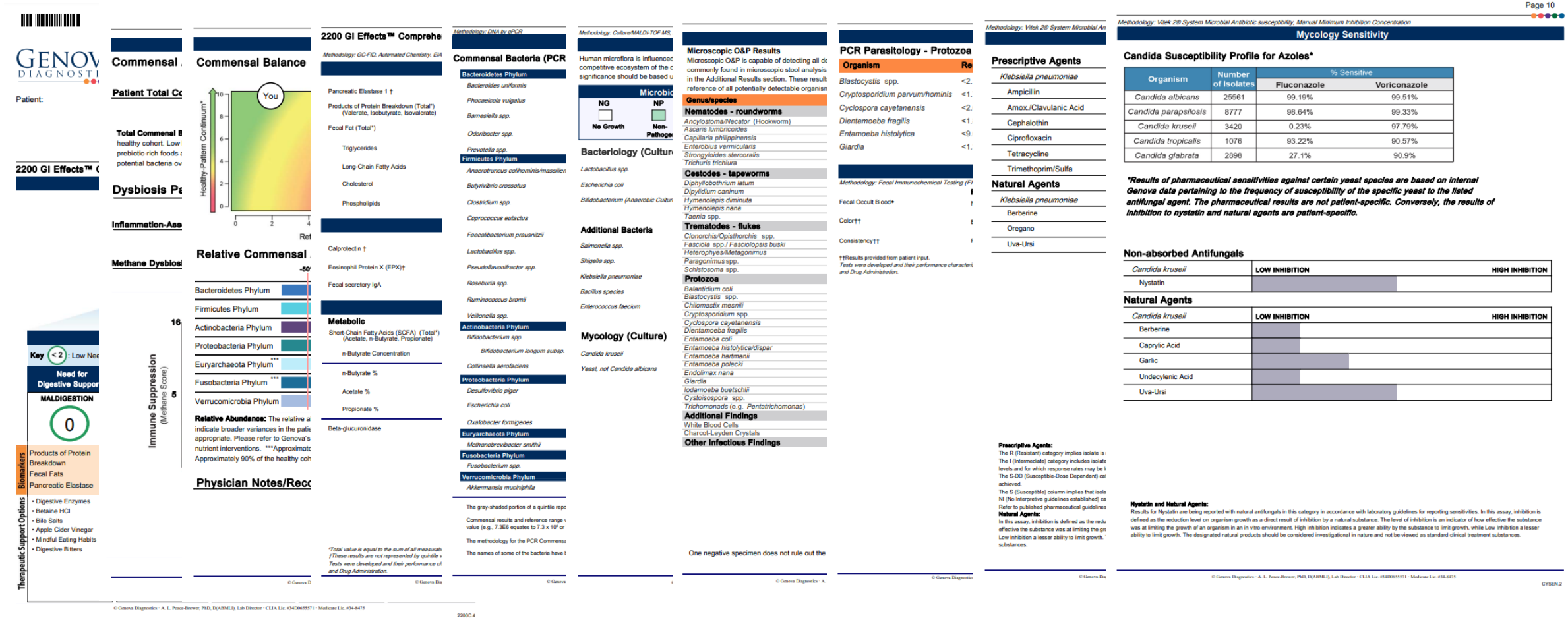
Case Study #5 – Summary

- Normal Shannon Diversity Index
- No overt pathogens
- Elevation in potential to make TMA and Hydrogen Sulfide gas

- No physical complaints
- Looking to optimize health and mitigate family history risks

- Increase dietary intake cruciferous vegetables
- Resistant starches, FOS

GI Effects Comprehensive Stool Profile



Patient:

2200 GI Effects™

Commensal Balance

You

Healthy-Pattern Continuum*

Relative Commensal

Bacteroidetes Phylum
Firmicutes Phylum
Actinobacteria Phylum
Proteobacteria Phylum
Euryarchaeota Phylum
Fusobacteria Phylum
Verrucomicrobia Phylum

Relative Abundance: The relative al
indicate broader variances in the patie
appropriate. Please refer to Genova's
nutrient interventions. ***Approximate
Approximately 90% of the healthy coh

Physician Notes/Recc

2200 GI Effects™ Comprehe

Methodology: GC-FID, Automated Chemistry, EIA

Pancreatic Elastase 1 †

Products of Protein Breakdown (Total*)
(Valerate, Isobutyrate, Isovalerate)

Fecal Fat (Total*)

Triglycerides

Long-Chain Fatty Acids

Cholesterol

Phospholipids

Calprotectin †

Eosinophil Protein X (EPX)†

Fecal secretory IgA

Metabolic

Short-Chain Fatty Acids (SCFA) (Total*)
(Acetate, n-Butyrate, Propionate)

n-Butyrate Concentration

n-Butyrate %

Acetate %

Propionate %

Beta-glucuronidase

*Total value is equal to the sum of all measurabl
†These results are not represented by quintile v
Tests were developed and their performance ch
and Drug Administration.

Methodology: DNA by qPCR

Commensal Bacteria (PCR

Bacteroidetes Phylum
Bacteroides uniformis
Phocaeicola vulgatus
Barnesiella spp.
Odoribacter spp.
Prevotella spp.
Firmicutes Phylum
Anaerotruncus colihominis/massilien
Butyrivibrio crossotus
Clostridium spp.
Coprococcus eutactus
Faecalibacterium prausnitzii
Lactobacillus spp.
Pseudoflavonifractor spp.
Roseburia spp.
Ruminococcus bromii
Veillonella spp.
Actinobacteria Phylum
Bifidobacterium spp.
Bifidobacterium longum subsp.
Collinsella aerofaciens
Proteobacteria Phylum
Desulfovibrio piger
Escherichia coli
Oxalobacter formigenes
Euryarchaeota Phylum
Methanobrevibacter smithii
Fusobacteria Phylum
Fusobacterium spp.
Verrucomicrobia Phylum
Akkermansia muciniphila

The gray-shaded portion of a quintile repo

Commensal results and reference range v
value (e.g., 7.3E6 equates to 7.3 x 10⁶ or

The methodology for the PCR Commensa

The names of some of the bacteria have t

Methodology: Culture/MALDI-TOF MS,

Human microflora is influence
competitive ecosystem of the
significance should be based u

Microbic

NG: No Growth
NP: Non-Pathoge

Bacteriology (Cultur

Lactobacillus spp.
Escherichia coli
Bifidobacterium (Anaerobic Cultur

Additional Bacteria

Salmonella spp.
Shigella spp.
Klebsiella pneumoniae
Bacillus species
Enterococcus faecium

Mycology (Culture)

Candida krusei
Yeast, not Candida albicans

Microscopic O&P Results

Microscopic O&P is capable of detecting all d
commonly found in microscopic stool analysis
in the Additional Results section. These result
reference of all potentially detectable organism

Genus/species

Nematodes - roundworms
Ancylostoma/Necator (Hookworm)
Ascaris lumbricoides
Capillaria philippinensis
Enterobius vermicularis
Strongyloides stercoralis
Trichuris trichiura

Cestodes - tapeworms
Diphyllobothrium latum
Dipylidium caninum
Hymenolepis diminuta
Hymenolepis nana
Taenia spp.

Trematodes - flukes
Clonorchis/Opisthorchis spp.
Fasciola spp./ Fasciolopsis buski
Heterophyes/Metagonimus
Paragonimus spp.
Schistosoma spp.

Protozoa
Balantidium coli
Blastocystis spp.
Chilomastix mesnili
Cryptosporidium spp.
Cyclospora cayetanensis
Dientamoeba fragilis
Entamoeba coli
Entamoeba histolytica/dispar
Entamoeba hartmanii
Entamoeba polecki
Endolimax nana
Giardia
Iodamoeba buetschlii
Cystoisospora spp.
Trichomonads (e.g. Pentatrichomonas)

Additional Findings
White Blood Cells
Charcot-Leyden Crystals

Other Infectious Findings

One negative specimen does not rule out the

PCR Parasitology - Protozoa

Organism	Re
Blastocystis spp.	<2.
Cryptosporidium parvum/hominis	<1.
Cyclospora cayetanensis	<2.
Dientamoeba fragilis	<1.
Entamoeba histolytica	<9.
Giardia	<1.

Methodology: Fecal Immunochemical Testing (FI

Fecal Occult Blood*
Color††
Consistency††

††Results provided from patient input.
Tests were developed and their performance characteris
and Drug Administration.

Methodology: Vitek 2® System Microbial An

Prescriptive Agents

Klebsiella pneumoniae
Ampicillin
Amox./Clavulanic Acid
Cephalothin
Ciprofloxacin
Tetracycline
Trimethoprim/Sulfa

Natural Agents

Klebsiella pneumoniae
Berberine
Oregano
Uva-Ursi

Prescriptive Agents:
The R (Resistant) category implies isolate is
The I (Intermediate) category includes isolat
levels and for which response rates may be l
The S-DD (Susceptible-Dose Dependent) ca
achieved.
The S (Susceptible) column implies that isola
NI (No Interpretive guidelines established) ca
Refer to published pharmaceutical guidelines
Natural Agents:
In this assay, inhibition is defined as the redu
effective the substance was at limiting the gr
Low Inhibition a lesser ability to limit growth.
substances.

Page 10

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

Mycology Sensitivity

Candida Susceptibility Profile for Azoles*

Organism	Number of Isolates	% Sensitive	
		Fluconazole	Voriconazole
Candida albicans	25561	99.19%	99.51%
Candida parapsilosis	8777	98.64%	99.33%
Candida kruseii	3420	0.23%	97.79%
Candida tropicalis	1076	93.22%	90.57%
Candida glabrata	2898	27.1%	90.9%

*Results of pharmaceutical sensitivities against certain yeast species are based on internal Genova data pertaining to the frequency of susceptibility of the specific yeast to the listed antifungal agent. The pharmaceutical results are not patient-specific. Conversely, the results of inhibition to nystatin and natural agents are patient-specific.

Non-absorbed Antifungals

Candida kruseii	LOW INHIBITION	HIGH INHIBITION
Nystatin		

Natural Agents

Candida kruseii	LOW INHIBITION	HIGH INHIBITION
Berberine		
Caprylic Acid		
Garlic		
Undecylenic Acid		
Uva-Ursi		

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.

Immune Suppression (Methane Score)

Key < 2 : Low Nee

Need for Digestive Suppor

MALDIGESTION

0

Biomarkers
Products of Protein Breakdown
Fecal Fats
Pancreatic Elastase

Therapeutic Support Options
- Digestive Enzymes
- Betaine HCl
- Bile Salts
- Apple Cider Vinegar
- Mindful Eating Habits
- Digestive Bitters

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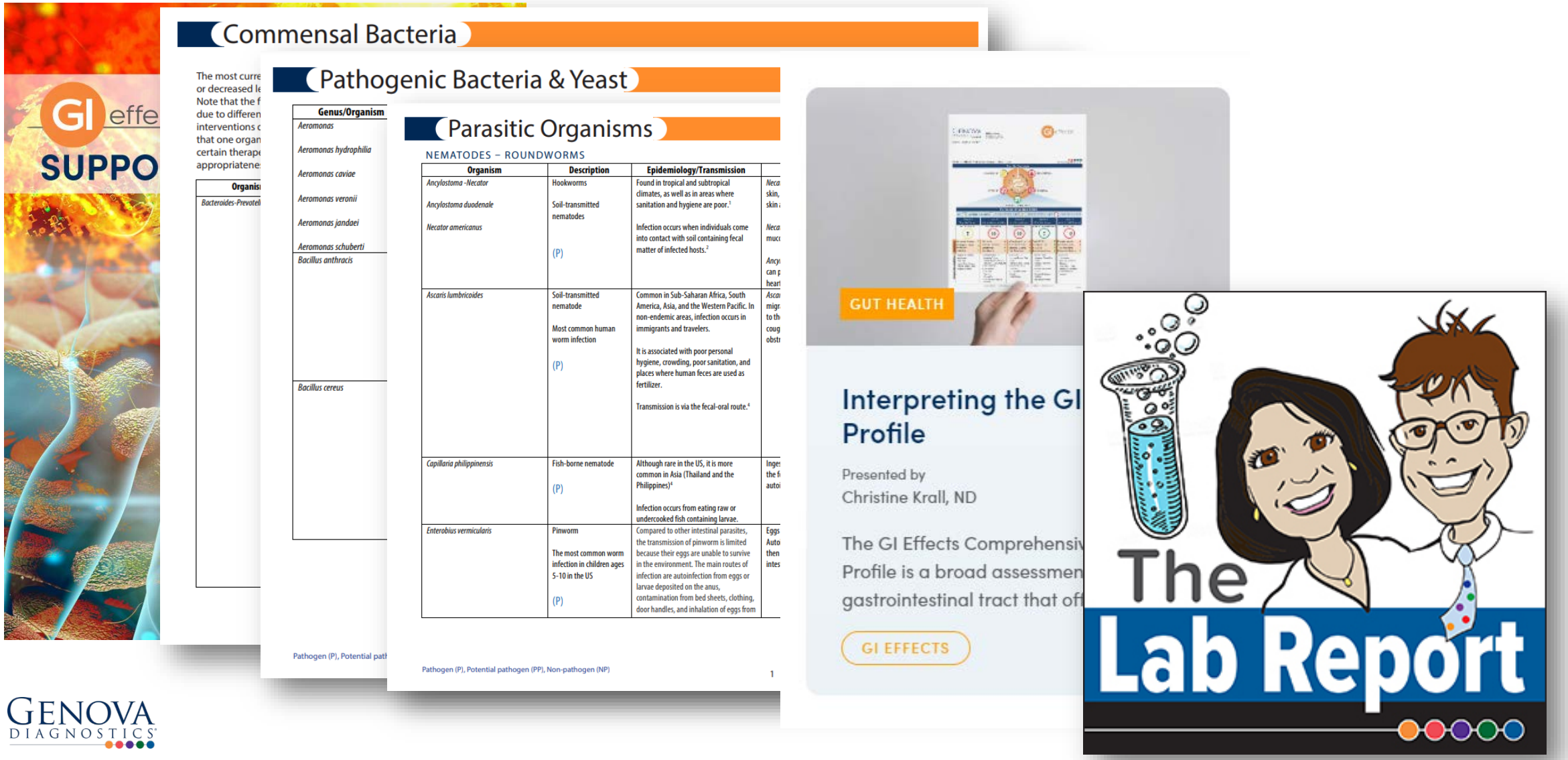
2200C.4

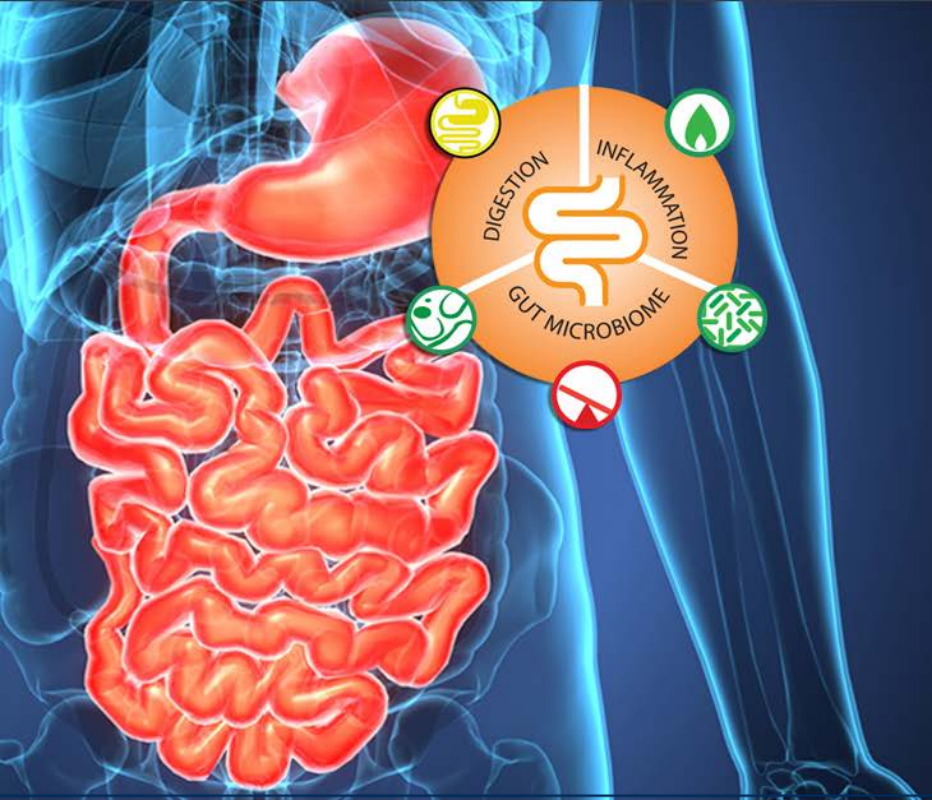
CYSEN.2

GENOVA DIAGNOSTICS

Support Materials



GENOVA DIAGNOSTICS



The GI Effects Comprehensive Stool Profile

Implementation: From Testing to Treatment

Patricia M. Devers, DO
Chief Clinical Officer | Genova Diagnostics