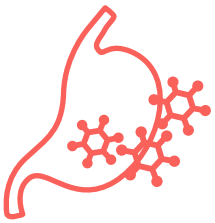
What Can Clinicians and Patients Expect from Healthpath Gut Health Testing?

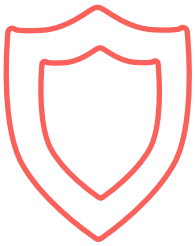
The Healthpath Gut Test shows you what's going on in your gut. By looking at imbalances in bacteria, yeasts, parasites and other intestinal health biomarkers, you find out what's contributing to your symptoms. You also receive targeted diet, supplement and lifestyle recommendations to help you take back control.

The biomarkers provide clinical information on three key areas:



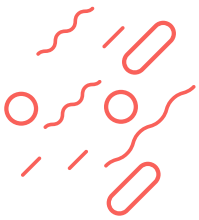
1 | Digestion/Absorption

- pH
- Pancreatic elastase
- Zonulin



2 | Immune activity/Inflammation

- Calprotectin
- Haemoglobin
- Secretory IgA
- H. Pylori
- Archaea/methanogens
- E. Coli, Lactobacillus species, Enterococcus species
- Akkermansia muciniphila, Faecalibacterium prausnitzii



3 | Gut Microbiome/Mycobiome

- Microbiome diversity
- Enterotype
- Dysbiosis index
- Actinobacteria
- Bacteroidetes
- Firmicutes
- Proteobacteria
- Fusobacteria
- Verrucomicrobia
- Hydrogen-sulphide production
- Oxalate-degrading bacteria
- Yeasts/moulds
- Parasites
- Helminths

Clinical Advantages of The Healthpath Gut Health Test qPCR Technology

This new method of analysis allows for a single sample. This makes the process easier for everyone, and it's particularly helpful for children and those struggling with diarrhoea or constipation.

	Gut Health Test	Advanced Gut Health Test Pro
Stool properties		
Colour	✓	✓
Consistency	✓	✓
pH	✓	✓

Diversity:
Your diversity is key, which is why our microbiome analysis covers hundreds of parameters. High bacterial diversity is known to protect against intestinal infections. But low bacterial diversity is common, especially in disease states or after a course of antibiotics. When diversity is low, opportunistic bacteria like pathogens, fungi and viruses can proliferate.

Rather than focusing on individual species, it's more important to investigate how the different bacteria interact. Together, they're responsible for a host of intestinal functions.

	Gut Health Test	Advanced Gut Health Test Pro
Biodiversity		
Diversity	✓	✓
Dysbiosis index	✓	✓

There are four large phyla (groups) of bacteria: Bacteroidetes, Firmicutes, Actinobacteria and Proteobacteria. We also report on two smaller, clinically relevant phyla: Verrucomicrobia and Fusobacteria.

	Gut Health Test	Advanced Gut Health Test Pro
Bacterial distribution		
Actinobacteria	✓	✓
Bacteroidetes	✓	✓
Firmicutes	✓	✓
Fusobacteria	✓	✓
Proteobacteria	✓	✓
Verrucomicrobia	✓	✓
Other	✓	✓
Firmicutes/ Bacteroidetes Ratio	✓	✓

Enterotype:
Recent research suggests there are three different types of gut microbiomes, known as 'enterotypes'. Not only do the different enterotypes influence the absorption of minerals, but they also have different metabolic properties.

Enterotype 1 has high levels of Bacteroides species, which use fat and protein effectively. Enterotype 2 has a strong Prevotella population, which is better at metabolising carbohydrates. Enterotype 3 is the rarest enterotype. It has high levels of Ruminococcus flora, though we don't yet know which macronutrients it prefers.

Enterotypes aren't affected by a person's age or gender and they remain stable for years. They can be influenced, however, by a long-term change of diet and by taking prebiotics.

	Gut Health Test	Advanced Gut Health Test Pro
Enterotype		
1, 2 or 3	✓	✓

	Gut Health Test	Advanced Gut Health Test Pro
Actinobacteria		
Bifidobacteria	✓	✓
Equol-producing bacteria	✓	✓
Adlercreutzia species		✓
Eggerthella lenta		✓
Slackia species		✓

	Gut Health Test	Advanced Gut Health Test Pro
Bacteroidetes		
Bacteroides	✓	✓
Prevotella	✓	✓
Prevotella copri	✓	✓

	Gut Health Test	Advanced Gut Health Test Pro

Firmicutes:
Butyrate is a short-chain fatty acid that's produced by bacteria in the colon. It's quickly absorbed by the intestinal mucosa, which means the only reliable way to measure it is to look at the number of butyrate-producing bacteria.

Firmicutes bacteria are key butyrate producers. One of these, Faecalibacterium prausnitzii, typically makes up 5–15% of human intestinal bacteria. This important butyrate-producing species has anti-inflammatory properties—so much so that an absence of Faecalibacterium prausnitzii typically correlates with higher levels of inflammation.

Firmicutes		
Butyrate-producing bacteria	✓	✓
Faecalibacterium prausnitzii	✓	✓
Eubacterium rectale	✓	✓
Eubacterium hallii	✓	✓
Roseburia species	✓	✓
Ruminococcus species	✓	✓
Coprococcus	✓	✓
Butyrivibrio species		✓
Cl. butyricum		✓
Total bacterial count	✓	✓
Clostridia	✓	✓
Clostridia total bacterial count	✓	✓
Clostridia cluster 1	✓	✓
Clostridia histolytium		✓
Clostridium perfringens		✓
Clostridium sporenges		✓
Other		✓
Christensenellaceae		✓
Dialister invisus		✓

Fusobacteria		
Fusobacterium species	✓	✓

Verrucomicrobia		
Akkermansia muciniphila	✓	✓

	Gut Health Test	Advanced Gut Health Test Pro

Proteobacteria		
Potentially pathogenic bacteria	✓	✓
Haemophilus	✓	✓
Acinetobacter	✓	✓
Escherichia coli biovare	✓	✓
Proteus species	✓	✓
Proteus mirabilis		✓
Klebsiella species	✓	✓
Klebsiella pneumoniae		✓
Enterobacter species	✓	✓
Serratia species	✓	✓
Hafnia species	✓	✓
Morganella species	✓	✓
Campylobacter species		✓
Providencia species		✓
Citrobacter species		✓
Histamine-producing bacteria	✓	✓
H2S production	✓	✓

Hydrogen-sulphide production:
Bacterial metabolism isn't always a good thing. Some bacteria reduce sulphate to create hydrogen sulphide—a toxic metabolic by-product that can damage the gut lining. The species Bilophila wadsworthii, Desulfomonas pigra and Desulfovibrio piger are thought to be potent hydrogen-sulphide developers.

Sulphate-reducing bacteria	✓	✓
Desulfovibrio piger		✓
Desulfomonas pigra		✓
Bilophila wadsworthii		✓
Oxalate-degrading bacteria		✓
Oxalobacter formigenes		✓

Archaea:
Archaea have been overlooked in microbiome studies until recently. New research suggests that 1) archaea are part of the microbiome in plants, animals and humans, 2) they form biofilms and 3) they interact with the human immune system. Some archaea are also methanogens, which may play a role in chronic constipation.

Archaea		
Methanobrevibacter	✓	✓

	Gut Health Test	Advanced Gut Health Test Pro
Immunogenically effective bacteria		
Escherichia coli	✓	✓
Enterococcus species	✓	✓
Lactobacillus species	✓	✓

Mucin production/mucosal barrier:
A healthy colon has a protective mucous layer. If this layer is damaged—or only small amounts of mucous are produced—pathogens, pollutants and allergens can come into direct contact with the mucosa. This leads to inflammation.

The bacterium Akkermansia muciniphila is important because it encourages goblet cells to produce this protective mucous. Parts of this mucous also provide a special type of carbohydrate called oligosaccharides, which feed the bacteria that make gut-healing butyrate. With the right bacteria, it becomes a virtuous circle!

Mucin production/ mucosal barrier		
Akkermansia muciniphila	✓	✓
Faecalibacterium prausnitzii	✓	✓
Yeasts/moulds		
Candida albicans	✓	✓
Candida species	✓	✓
Geotrichum candidum	✓	✓
Moulds	✓	✓
Functional markers		
Calprotectin	✓	✓
Haemoglobin in faeces immunologically	✓	✓
Secretory IgA	✓	✓
Pancreatic elastase	✓	✓
Zonulin		✓

Parasites:
The Multiplex Real-time PCR (Multiplex quantitative real-time PCR) is a faster and more effective method for detecting parasites. This new test:
- provides reliable analysis, even with minimal attack
- gives no false positives with non-pathogens
- can be sent out with regular mail
- gives reliable results in symptom-free patients and also after treatment

	Gut Health Test	Advanced Gut Health Test Pro
Parasites		
Pathobionts	✓	✓
Blastocystis hominis	✓	✓
Dientamoeba fragilis	✓	✓
Helicobacter AG	✓	✓
Pathogenic intestinal protozoa	✓	✓
Giardia lamblia	✓	✓
Entamoeba histolytica	✓	✓
Cryptosporidium species	✓	✓
Cyclospora cayetanensis	✓	✓
Helminths **COMING SOON**		✓
Taenia species		✓
Taenia solium		✓
Taenia saginata		✓
Ascaris species		✓
Enterobius vermicularis		✓
Ancylostoma species		✓
Ancylostoma duodenale		✓
Hymenolepsis species		✓
Hymenolepsis nana		✓
Hymenolepsis diminuta		✓
Trichuris trichiura		✓
Necator americanus		✓
Strongyloides species		✓
Strongyloides stercoralis		✓
Microsporidia		✓
Enterocytozoon species		✓
Encephalitozoon species		✓

GUT HEALTH M.O.T

EXAMPLE TEST REPORT

Thank you for taking the Gut Health MOT Test. We're delighted to provide your personalised report.

The report is divided into four sections:

I. **Your microbiome**
This provides insight into the consistency of your poop, the diversity of your bacteria, your 'enterotype' and your dysbiosis index. These are all important and interconnected components that shed light on the health of your digestive system.

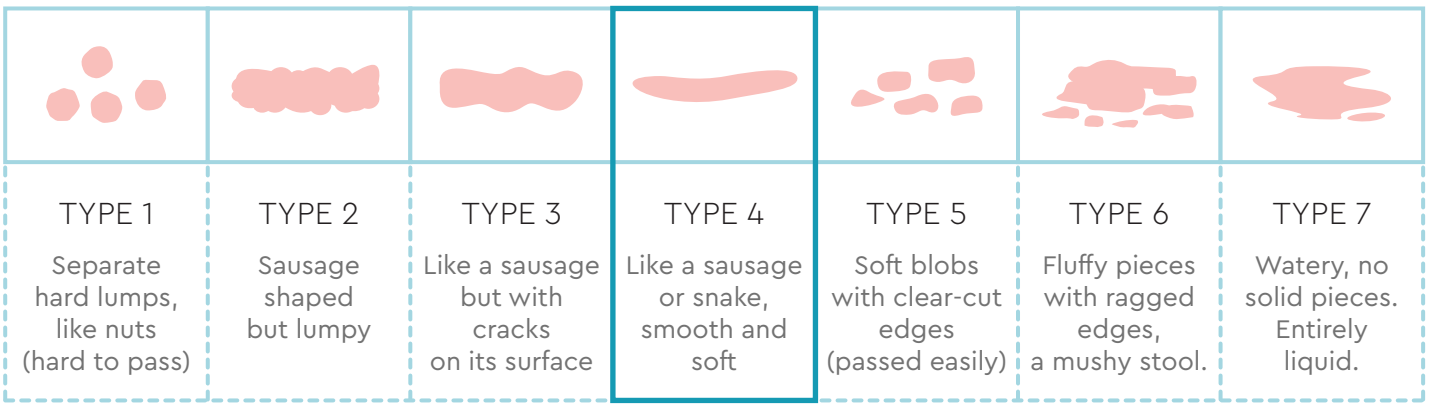
II. **Bacteria, yeasts and/or parasites**
This section gives details of organisms that have been detected in your digestive system.

III. **Biomarkers**
These assess both your ability to break down and absorb your food, and any immune system activity. This helps us understand whether food sensitivities or gut infections are contributing to your symptoms.

IV. **Recommendations**
Finally, this section provides your lifestyle and supplement recommendations.

I. YOUR MICROBIOME

Consistency



TYPE 1	TYPE 2	TYPE 3	TYPE 4	TYPE 5	TYPE 6	TYPE 7
Separate hard lumps, like nuts (hard to pass)	Sausage shaped but lumpy	Like a sausage but with cracks on its surface	Like a sausage or snake, smooth and soft	Soft blobs with clear-cut edges (passed easily)	Fluffy pieces with ragged edges, a mushy stool.	Watery, no solid pieces. Entirely liquid.

OPTIMAL

Decreased water activity, associated with harder stools and prolonged transit time, is thought to limit bacterial growth by reducing nutrient mobility and enzyme activity.

Species richness (the number and types of bacteria in the gut) is known to decline with higher BSS scores, reaching its minimum in those with loose stools (type 7).

pH

6.0

ACIDIC **OPTIMAL** NEUTRAL ALKALINE

3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0

YOU

pH is all about balance.
Both very acidic and very alkaline scores represent unhealthy digestive systems.

A **LOW** pH can indicate that carbohydrates aren't being absorbed properly.

A **HIGH** pH suggests inadequate acid production and digestion.

Biodiversity

Congrats!
You are quite inhabited.

Species richness is thought to be a major marker for gut health. Ideally, we all want high bacterial richness and diversity, as these often reflect ecosystem stability and resilience.

There's also an association between a reduction in the number of species in a person's poop sample and an increased risk of disease.

What can decrease biodiversity?
Some factors are transit time, antibiotic therapies, infections, increasing age, unbalanced diets (low in fibre), smoking.

Enterotype

Recent research suggests that the human microbiome can be assigned to three main groups, known as 'enterotypes'.

Your result

Enterotype 1

Enriched with Bacteroides and the co-occurring Parabacteroides

Enterotype 2

Enriched with Prevotella and the co-occuring Desulfovibrio

Enterotype 3

Enriched with Ruminococcus and the co-occurring Akkermansia

Dysbiosis index

0 5 10 15 20 25 30

OPTIMAL

Your result

The dysbiosis index is a measure of deviations within the microbiome. In other words, if you have too much of one type of bacteria, or not enough of another, it can affect your index.

II. BACTERIA, FUNGI AND PARASITES

Firmicutes	HIGH

What Is It? The phylum (family) Firmicutes is a group of Gram-positive bacteria. Out of thousands of bacterial species inhabiting the human gut, the majority belong to two dominant families, the Bacteroidetes and Firmicutes.

What Is Their Significance? Firmicutes are a normal inhabitant of the microbiome. In patients with IBD, the number of bacteria belonging to the phyla Firmicutes and Bacteroidetes have been found to be decreased. In obesity, there appears to be a trend towards greater relative abundance of Firmicutes. It is worth noting though that several species within the phylum Firmicutes ferment complex carbohydrates in the colon and produce butyrate, which has potential barrier-protecting functions and are thought to have a direct anti-inflammatory effect in the gut, meaning it helps prevent leaky gut.

Verrucomicrobia	LOW

What is it? A genus (group) of bacteria. They're normal residents of a healthy microbiome.

Why's it significant? Akkermansia is the sole intestinal representative of the verrucomicrobia in human stools. Verrucomicrobia are generally found to be higher in vegetarians rather than omnivores.

Firmicutes/Bacteroidetes	HIGH

What Is It? This is a ratio between the two main phyla/families of bacteria, firmicutes and bacteriodetes

What Is The Significance Of The Ratio?: Firmicutes and bacteriodetes make up to 90% of our micorbiome. The ratio has been of interest to researchers recently as obesity has been characterised by an altered intestinal Firmicutes:Bacteroidetes ratio, with greater relative abundance of Firmicutes, although this hasn't always been found. One study in children found a correlation between elevated firmicutes and inflammation in the body. Also IBD patients tend to have less bacterial diversity as well as lower numbers of Firmicutes - which together may contribute to reduced concentrations of microbial-derived butyrate. Butyrate is thought to have a direct anti-inflammatory effect in the gut.

II. BACTERIA, FUNGI AND PARASITES

Bacteroides — LOW

What is it? A genus (group) of bacteria that makes up a large portion of a normal gut microbiome.

Why's it significant? Bacteroides are immune-modulating bacteria. They're believed to be involved in microbial balance, the integrity of the gut wall and neuro-immune health. They're more prevalent in people who consume animal-based diets. People with low levels of bacteroides may be more likely to experience gut inflammation.

Faecalibacterium prausnitzii — LOW

What is it? A species of bacteria. It's one of the most plentiful types of bacteria in the gut microbiome.

Why's it significant? Appropriate levels of Facecalibacterium prausnitzii (F. prausnitzii) are generally seen as a marker of health, once when its population is altered (decreased), inflammatory processes are favored. It's believed to be a key producer of butyrate, which is a short-chain fatty acid that helps to reduce inflammation and heal the gut. Levels of F. prausnitzii can be lower in patients suffering from intestinal and metabolic disorders such as inflammatory bowel diseases (IBD), irritable bowel syndrome (IBS), colorectal cancer (CRC), obesity and coeliac disease.

Eubacterium rectale — LOW

What is it? A species of bacteria. It's commonly found in the gut microbiome.

Why's it significant? Eubacterium rectale (E. rectale) produces butyrate, a short-chain fatty acid that helps to reduce inflammation and heal the gut. It makes sense that E. rectale has been found to be lower in people who suffer from ulcerative colitis. On the other hand, certain subspecies of E. rectale have also been associated with lower gut diversity, higher BMI and high blood fasting insulin levels.

III. BIOMARKERS

Eubacterium hallii	LOW

What is it? A species of bacteria. It makes up 2–3% of the community found in human faeces (poop).

Why's it significant? Eubacterium hallii (E. hallii) is considered an important indicator of metabolic balance within the intestines. It produces butyrate, a short-chain fatty acid that helps to reduce inflammation and heal the gut. Pre-clinical trials show that it may help inflammatory and metabolic disorders, while animal studies show it may improve insulin sensitivity. E. hallii also helps to produce vitamin B12, though it's unlikely much of this is absorbed by the body.

Roseburia spp.	LOW

What is it? Several species of bacteria. They're part of a normal gut microbiome.

Why's it significant? Roseburia species produce butyrate, a short-chain fatty acid that helps to reduce inflammation and heal the gut. Lower levels of Roseburia species have been observed in people suffering from inflammatory bowel disease, including ulcerative colitis. Along with Faecalibacterium prausnitzii, low levels of Roseburia species have also been seen in worsening kidney disease. Higher levels of Roseburia species have been associated with weight loss and improved glucose tolerance.

Clostridia total bacterial count	HIGH

What is it? A class of bacteria. They're part of a normal gut microbiome.

Why's it significant? Clostridia can be both friendly and unfriendly. Friendly types help to maintain overall gut function by supporting the immune system and producing butyrate, a short chain fatty acid that provides fuel for intestinal cells (as well as reducing inflammation). The not-so-friendly types of Clostridia (which include Clostridium botulinum, Clostridium tetani and Clostridium difficile) have been associated with various conditions, from diarrhoea to autism.

II. BACTERIA, FUNGI AND PARASITES

Akkermansia muciniphila — LOW

What is it? One of the most plentiful single species in the gut microbiome. It makes up 0.5–5% of the total bacteria.

Why's it significant? Higher levels of Akkermansia muciniphila (A. muciniphila) have been associated with greater metabolic health. Lower A. muciniphila, on the other hand, has been associated with obesity, diabetes, cardiometabolic diseases and low-grade inflammation. A. muciniphila breaks down mucins (a part of mucous in the intestines) to produce short-chain fatty acids. These short-chain fatty acids help to feed the host (that's you!) as well as other bacteria in the intestines.

Sulphate reducing bacteria — HIGH

What is it? Certain bacteria in the colon use the compound sulphate (found in lots of foods) to produce hydrogen sulphide. These bacteria include:

- Bilophila wadsworthii
- Desulfomonas pigra
- Desulfovibrio piger

Why's it significant? Although sulfate/sulfite-reducing bacteria are positively associated with inflammation, both pro- and anti-inflammatory signaling have been attributed to hydrogen sulphide.

Methanobrevibacter — HIGH

What is it? A type of archaea. Archaea constitute the domain of single-celled microorganisms, and are thus slightly different to bacteria. They are prokaryotes, meaning they have no cell nucleus.

Why's it significant? Methanogens such as Methanobrevibacter spp. belong to the domain of the archaea and are not bacteria. In humans, a stable colonisation is found in the gastrointestinal tract and oral cavity, in the vagina and on the skin. Methanogens are able to convert hydrogen to methane, hence are often referred to as methanogens. The frequency of methanogens is related to various diseases. Increased methanogenesis can reduce intestinal motility and promote constipation-type irritable bowel syndrome. Increased methanogenesis is also reported for Diverticulosis patients.

Example Report

External ID

Name	**Demo**	Date of Birth	**26.04.1979**	Order ID	
First Name	**Demo**	Sex	Male	Order Date	22.05.2019
Sampling Date	14.05.2019 12:45	Validation Date		Findings Status	**Final Report**
Sample Material	FE	Validation on	04.06.2019	Findings Date	04.06.2019

Test	Result	Unit	Standard Range	Previous Result	Result Material Method
Stool Diagnostics					
Microbiome Healthpath Maxi					
Moleculargenetic Microbiomeanalysis MAXI					
Stool Properties					
Colour	lightbrown				FE NA) VISU
Consistency	mushy				FE NA) VISU
pH	6,0		5,8 - 6,5		FE NA) TESTS
Biodiversity					
Diversity	6,22		> 5,0		FE NA) MGSEQ

The bacterial diversity in the intestinal tract may vary considerably from person to person. Antibiotic therapies, infections, increasing age, unbalanced diets or smoking are causes of declining diversity.

Grad **6**

Bacteria Phyla (Distribution)					
Actinobacteria	2,5	%	1,0 - 5		FE NA) MGSEQ
Bacteroidetes	30,2	%	30 - 60		FE NA) MGSEQ
Firmicutes	45,4	%	30 - 60		FE NA) MGSEQ
Fusobacteria	0,0	%	0,0 - 1,0		FE NA) MGSEQ
Proteobacteria	**9,5**	%	1,5 - 5,0		FE NA) MGSEQ
Verrucomicrobia	**0,1**	%	1,5 - 5		FE NA) MGSEQ
Other	12,1	%			FE NA) MGSEQ
Ratio					
Firmicutes/Bacteroidetes	**1,51**	Quotient	< 1,5		FE NA) RECHN
Enterotype					
Prevotella					FE NA) MGSEQ

Human intestinal microbiomes can be differentiated into three Enterotypes. Enterotypes are defined by dominant bacterial clusters with distinct metabolic properties.

Enterotyp **2**

Dysbiosis index

FE=Stuhl

* cooperate analytics (R), A) accredited, NA) not accredited

Name	**Demo**	Date of Birth	**26.04.1979**	Order ID	
First Name	**Demo**	Sex	Male	Order Date	22.05.2019

Test	Result	Unit	Standard Range	Previous Result

The dysbiosis index represents a measure of deviations within the microbiome. Depending on their relevance, all detected phyla, genera and species are considered.

Index **19**

Bacteria Phyla - most important genera and species

Actinobacteria

Bifidobacteria	**1,2 x 10^8**	CFU/g faeces	> 5,0 x 10^9	
Bifidobacterium adolescentis	67	%		
Equol producing bacteria	2,5 x 10^10	CFU/g faeces	> 5,0 x 10^9	
Adlercreutzia spp.				
Eggerthella lenta				
Slackia. spp.				

Bacteroidetes

Bacteroides	**3,4 x 10^10**	CFU/g faeces	> 1,5 x 10^11	
Bacteroides uniformis	9	%		
Bacteroides ovatus	5	%		
Prevotella	1,6 x 10^11	CFU/g faeces	> 1,0 x 10^10	

Firmicutes

Butyrate producing bacteria

Faecalibacterium prausnitzii	6,5 x 10^10	CFU/g faeces	> 5,0 x 10^10	
Eubacterium rectale	**4,0 x 10^9**	CFU/g faeces	> 1,0 x 10^10	
Eubacterium hallii	**3,0 x 10^9**	CFU/g faeces	> 5,0 x 10^9	
Roseburia spp.	**6,7 x 10^8**	CFU/g faeces	> 2,0 x 10^10	
Ruminococcus spp.	3,2 x 10^10	CFU/g faeces	> 3,0 x 10^10	
Coprococcus	**1,3 x 10^10**	CFU/g faeces	> 2,0 x 10^10	
Butyrivibrio spp.	8,7 x 10^9	CFU/g faeces	> 5,0 x 10^9	
Cl. butyricum	1,6 x 10^10	CFU/g faeces	> 1,0 x 10^10	
Total bacterial count	**1,3 x 10^11**	CFU/g faeces	> 1,3 x 10^11	

Clostridia

Clostridia total bacterial count	3,1 x 10^9	CFU/g faeces	< 4,0 x 10^9	
Clostridia cluster I	3,7 x 10^8	CFU/g faeces	< 2,0 x 10^9	
Clostridium histolyticum	3,7 x 10^8	CFU/g faeces	< 2,0 x 10^9	
Clostridium perfringens	< 1,0 x 10^6	CFU/g faeces	< 1,0 x 10^8	
Clostridium sporogenes	< 1,0 x 10^6	CFU/g faeces	< 1,0 x 10^8	

Other

Christensenellaceae	6,1 x 10^9	CFU/g faeces	> 1,0 x 10^9	
Dialister invisus	< 1,0 x 10^6	CFU/g faeces	< 4,0 x 10^10	

Fusobacteria

Fusobacterium spp.	< 1,0 x 10^6	CFU/g faeces	< 1,0 x 10^7	

Verrucomicrobia

Akkermansia muciniphila	**< 1,0 x 10^6**	CFU/g faeces	> 5,0 x 10^9	

Proteobacteria

Pathogenic or potentially pathogenic bacteria

Haemophilus	4,1 x 10^7	CFU/g faeces	< 1,0 x 10^9	

FE=Stuhl

* cooperate analytics (R), A) accredited, NA) not accredited

Name	**Demo**	Date of Birth	**26.04.1979**	Order ID	
First Name	**Demo**	Sex	Male	Order Date	22.05.2019

Test	Result	Unit	Standard Range	Previous Result	Sample Material / Method
Acinetobacter	< 1,0 x 10^6	CFU/g faeces	< 1,0 x 10^6		FE NA) MGSEQ
Escherichia coli Biovare	< 1,0 x 10^4	CFU/g faeces	< 1,0 x 10^4		FE A) KULTAZ
Proteus species	< 1,0 x 10^4	CFU/g faeces	< 1,0 x 10^4		FE A) KULTAZ
Klebsiella species	< 1,0 x 10^4	CFU/g faeces	< 1,0 x 10^4		FE A) KULTAZ
Enterobacter species	< 1,0 x 10^4	CFU/g faeces	< 1,0 x 10^4		FE A) KULTAZ
Serratia species	< 1,0 x 10^4	CFU/g faeces	< 1,0 x 10^4		FE A) KULTAZ
Hafnia species	< 1,0 x 10^4	CFU/g faeces	< 1,0 x 10^4		FE A) KULTAZ
Morganella spp.	< 1,0 x 10^4	CFU/g faeces	< 1,0 x 10^4		FE NA) MIB
Histamine producing bacteria					
Histamine producing bacteria	< 1,0 x 10^6	CFU/g faeces	< 5,0 x 10^8		FE NA) MGSEQ
H2S production					
Sulphate reducing bacteria	**7,0 x 10^9**	CFU/g faeces	< 2,0 x 10^9		FE NA) MGSEQ
Desulfovibrio piger	< 1,0 x 10^6	CFU/g faeces	< 1,0 x 10^9		FE NA) MGSEQ
Desulfomonas pigra	< 1,0 x 10^6	CFU/g faeces	< 1,0 x 10^9		FE NA) MGSEQ
Bilophila wadsworthii	< 1,0 x 10^6	CFU/g faeces	< 2,0 x 10^9		FE NA) MGSEQ
Oxalate degrading bacteria					
Oxalobacter formigenes	1,1 x 10^9	CFU/g faeces	> 1,0 x 10^8		FE NA) MGSEQ
Archaea					
Methanobrevibacter	**3,4 x 10^8**	CFU/g faeces	< 1,0 x 10^8		FE NA) MGSEQ
Immunogenicity / Mucus production					
Immunogenically effective bacteria					
Escherichia coli	**1,0 x 10^5**	CFU/g faeces	10^6 - 10^7		FE A) KULTAZ
Enterococcus species	**< 1,0 x 10^4**	CFU/g faeces	10^6 - 10^7		FE A) KULTAZ
Lactobacillus species	**< 1,0 x 10^4**	CFU/g faeces	10^5 - 10^7		FE A) KULTAZ
Mucin production / Mucosa barrier					
Akkermansia muciniphila	**< 1,0 x 10^6**	CFU/g faeces	> 5,0 x 10^9		FE NA) MGSEQ
Faecalibacterium prausnitzii	6,5 x 10^10	CFU/g faeces	> 5,0 x 10^10		FE NA) MGSEQ
Yeasts / Molds					
Candida albicans	< 1,0 x 10^3	CFU/g faeces	< 1,0 x 10^3		FE A) KULTAZ
Candida species	< 1,0 x 10^3	CFU/g faeces	< 1,0 x 10^3		FE A) KULTAZ
Geotrichum candidum	< 1,0 x 10^3	CFU/g faeces	< 1,0 x 10^3		FE A) KULTAZ
Moulds	negative		negative		FE A) KULTAZ
Parasites					
Pathobionts					
Blastocystis hominis	positive		negative		FE NA) MOLEK
Dientamoeba fragilis	negative		negative		FE NA) MOLEK
Pathogenic intestinal protozoa					
Giardia lamblia	negative		negative		FE NA) MOLEK
Entamoeba histolytica	negative		negative		FE NA) MOLEK
Cryptosporidium spp.	negative		negative		FE NA) MOLEK
Cyclospora cayetanensis	negative		negative		FE NA) MOLEK
Colon Ca early detection					
Calprotectin	<17,9	mg/l	< 50		FE A) ELISA
Hemoglobin in feces immunologically	<10	µg/g	< 10		FE A) ELISA
Special Request					

FE=Stuhl

* cooperate analytics (R), A) accredited, NA) not accredited

Name	**Demo**	Date of Birth	**26.04.1979**	Order ID	
First Name	**Demo**	Sex	Male	Order Date	22.05.2019

Test	Result	Unit	Standard Range	Previous Result	Sample Material / Method
Secretory IgA	**<167**	µg/ml	510 - 2040		FE A) ELISA
Pancreatic elastase	240,45	µg/g	> 200		FE A) ELISA
Zonulin	**60,70**	ng/ml	< 55		FE A) ELISA
Gastro diagnostics					
Helicobacter AG	negative		negative		FE NA) CLIA

FE=Stuhl

* cooperate analytics (R), A) accredited, NA) not accredited

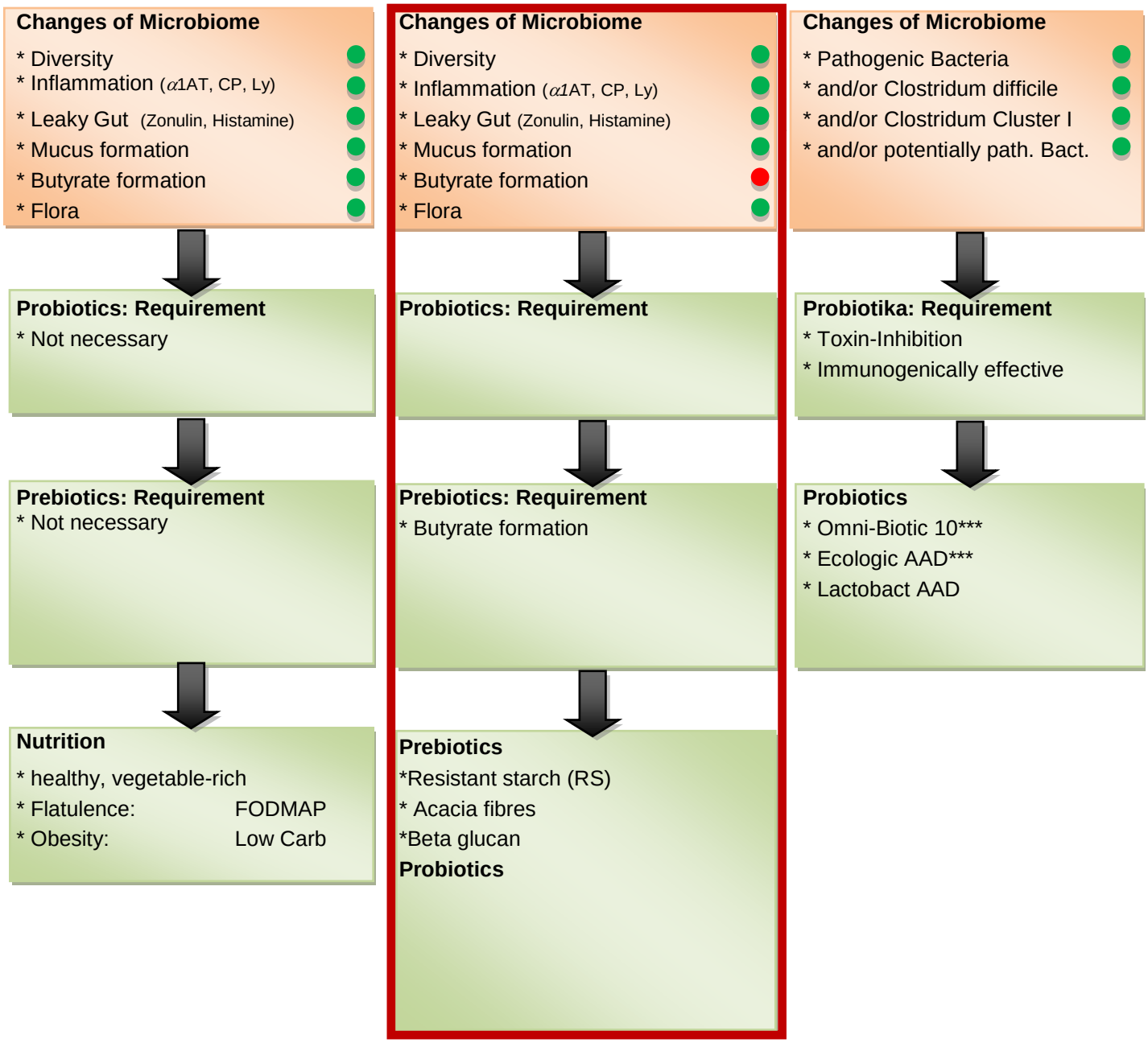
Demo Demo 26.04.1979

Overview - Results and Therapy Options

Dysbiose-Index 19

pH		
Enterotype	2	check vitamin B2, B5, C and biotin supply
Biodiversitiy		
Ratio Firmicutes/Bacteroidetes	↑	Low Carb Diet, prebiotics (scFOS/scGOS)*
Equol producing bacteria		
Butyrate producing bacteria	↓	prebiotics on the basis of resistant starch* or scFOS/scGOS*
Mucus production	↓	prebiotics (scFOS/scGOS)*
Mucosa integrity		
Milieu stabilising bacteria	↓	milieu stabilizing probiotics*, prebiotics (scFOS/scGOS)*
Immunogenic bacteria	↓	immunogenic effective probiotics*
Clostridia - total bacteria count		
Clostridia cluster I		
Fusobacteria		
Histamine producing bacteria		
H2S producing bacteria (SRB)	↑	fat and protein reduction, milieu stabilizing probiotics, prebiotics on the basis of
Potentially pathogenic bacteria		
Candida (facultive pathogenic)		
Oxalate degrading bacteria		

Therapy options with prebiotics and probiotics in overview

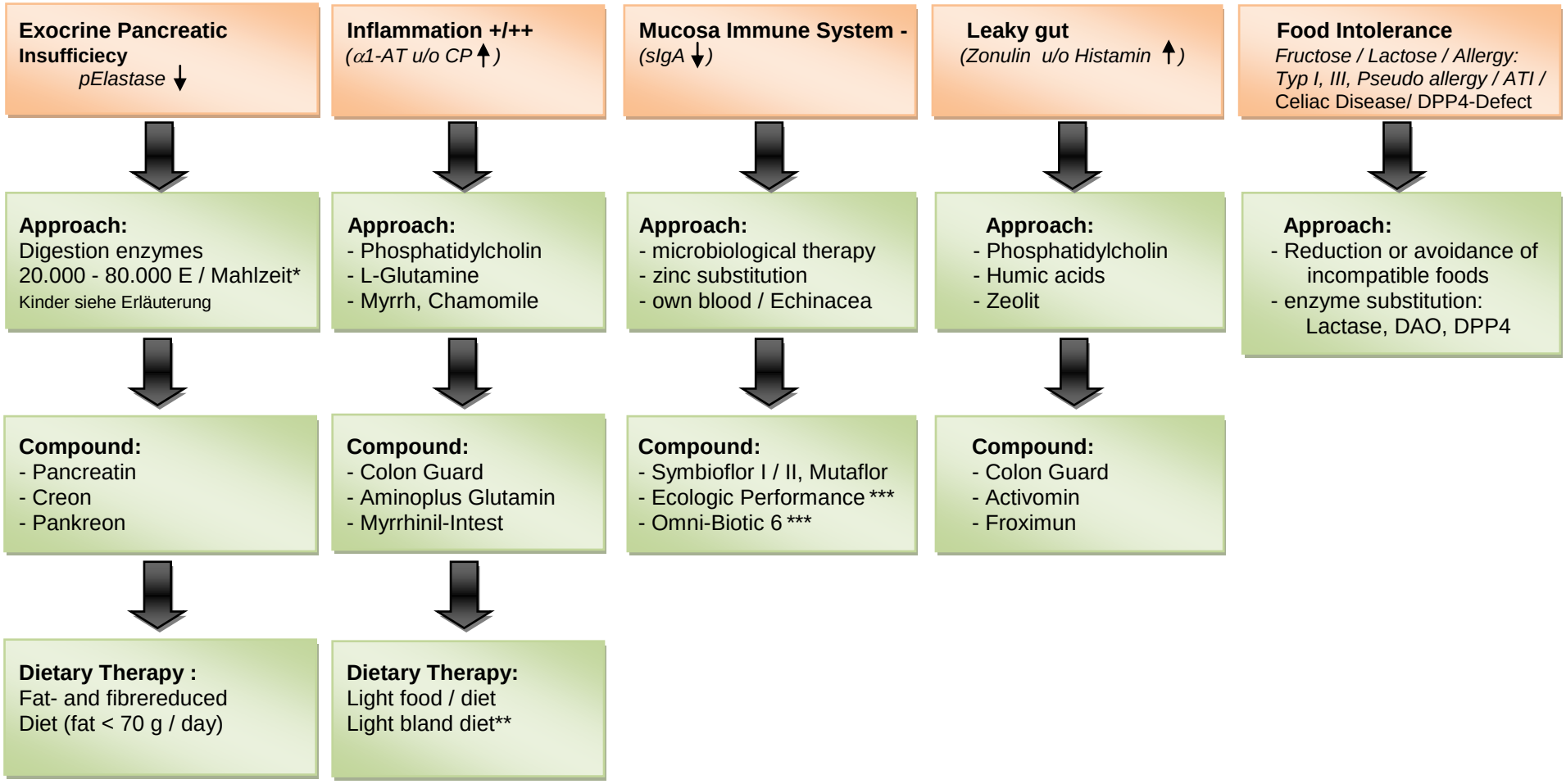


* age related: Omni-Biotic 60+ active

*** in combination with other probiotics

** age adapted: Lactobact 60plus

Therapy options based on results of pElastase, inflammation marker, sIgA and / or zonulin / histamine



* **Dosage** depending on fat content in stool, for **children** age and weight related dosages apply.
In case of slightly reduced pElastase values but normal fatty residues: possible administration of vegetable enzyme mixtures (e. g. Digest, Full Spectrum, Combizym).

** in case of α1-antitrypsin values > 100 mg / dl and / or calprotectin > 150 mg / l *** MIS-activating probiotics (alternatively see table „probiotics acc. to effects“)

Blastocystis hominis

Blastocystis is a parasite that is found throughout the world and is now considered the most common eukaryotic organism in the human intestinal tract. Evidence is often an expression of a transient, asymptomatic occurrence. In humans, 9 different subtypes have been detected so far, of which only a few (especially subtypes I and IV) are pathologically relevant. Depending on the source, the prevalence of Blastocystis in Central Europe ranges from 14 – 30 % of the population.

The examination on Blastocystis hominis is **positive**. Genetic material of the protozoa could be detected in the stool sample. Depending on the present colonization burden and the subtype, the evidence in the stool may also be associated with a symptomatic infection.

In this case, complementary therapies put focus on the administration of herbal extracts and/or yeast-based probiotics.

Attention: *According to the current state of knowledge, antibiotic treatment is indicated only in the case of persistent clinical symptoms, as it often shows high recurrence rates, leads to resistance and additionally affects the microbiome.*

Both antibiotic therapy and therapy with herbal extracts should always be supported by a simultaneous administration of probiotics with the aim of strengthening the patients microbiota.

Therapies

In vitro and in vivo studies have shown an inhibitory effect of various herbal extracts such as **oregano**, **garlic**, and **ginger oil**, as well as **black cumin extract** (Eida et al., 2016, Lepczyńska et al., 2017). In addition, probiotics based on ***Saccharomyces boulardii*** demonstrated efficacy comparable to antibiotics (Dinleyici et al., 2011).

Classic antibiotic therapies are mainly performed with metronidazole or iodoquinol. Resistance has been described for both antibiotic and herbal extract-based therapies.

Oregano oil has a blood-thinning effect, so people who take blood thinners should refrain from taking oregano oil. Preparations based on *Saccharomyces boulardii* (Saccharomyces cerevisiae HANSEN CBS 5926) are contraindicated in seriously ill or immunosuppressed patients.

Introduction

The **intestinal microbiome** (entirety of all bacteria living in the intestinal tract) has considerable influence on health or illness of humans. It modulates the immune defence, supplies the organism with vitamins (vitamin B1, B2, B6, B12, and K), participates in the digestion of food components, supplies intestinal epithelia with energy via developing short-chain fatty acids and stimulates intestinal peristalsis. The microbiome also plays an important role in the scope of xenobiotic detoxification. Shifts within the microbiome are causally relevant factors for diseases like adiposity, non-alcoholic fatty liver disease, diabetes, coronary heart disease or cancer. After the composition of the human intestinal microbiome was studied in more detail, alterations can be detected and counteracted with well-aimed measures.

Result Evaluation

With the help of the **molecular-genetic stool analysis,** the intestinal microbiome was analysed in order to assess the composition and to determine possible shifts. The evaluation yielded the following **results**:

Evaluation of Stool Consistency, Color and pH-Value

General viewing of the stool sample showed **mushy consistency**. Healthy stool should be mushy and formed. Liquid or slurry stool indicates accelerated, doughy or solid stool samples delayed intestinal passage.

The color of the analysed stool sample was brown. The **pH-value** was **within normal range** at 6.

Evaluation of the Intestinal Diversity

More important than individual bacteria species or types is the interaction of the bacteria present in the microbiome. Manifold tasks of the intestinal flora require adequate **diversity**. The intestinal diversity of humans may vary considerably.

In the microbiome of healthy people one finds **300 to 500 bacteria species**, in sick persons there are often a lot less. Causes for reduced diversity are manifold. They are for example repeated **antibiotic therapies, infections,** increasing **age, unbalanced diet** or **smoking**.

Research revealed that numerous diseases come along with reduced diversity and thus presumably promote disease manifestation. Very often reduced diversity is found in patients suffering from **adiposity, fatty liver** (NAF), **diabetes type 2, Alzheimer disease, chronic inflammatory bowel disease, intestinal cancer** or **irritable colon syndrome**. Due to decreasing diversity the intestinal microbiome no longer grants adequate protection against endogenic infections. Obese patients with reduced diversity tend to gain more weight, respond worse to diets and there are often already indications of fat metabolism disorders or insulin resistance. In patients suffering from chronic inflammatory bowel disease (CIBD) reduced diversity promotes recurrence and chronicity. Research data are also available for the irritable bowel syndrome, the manifestation of which is promoted by reduced diversity.

Result

The analysis indicates **adequate biodiversity**.

Frequency Scale of the Most Important Bacteria Phyla

The colon is populated by bacteria, which reach a total density of approximately 10^{11}-10^{12} bacterial cells/ml colon content. This dense community of bacteria consists mainly of three or four large bacteria phyla: **Bacteroidetes, Firmicutes, Actinobacteria** and **Proteobacteria**. Other phyla (Verrucomicrobia, Fusobacteria) show smaller shares.

In most cases 30-60 % of the microbiota are Bacteroidetes. The Firmicutes have the same share and mainly consist of Lachnospiraceae and Ruminococcaceae families. Actinobacteria have significantly lower bacteria counts. Mainly Bifidobacteria make up the Actinobacteria phylum. In the microbiome of healthy people Proteobacteria have a share of 1.5-5%, which can, however, after repeated antibiotic therapies or in case of inflammatory bowel diseases, increase significantly.

Result

The distribution of the bacteria-phyla shows a reduction of:

- Verrucomicrobia

Determination of the Firmicutes / Bacteroidetes Ratio

Patients suffering from **irritable bowel syndrome** or **obesity** often show a high share of Firmicutes.

Obesity increases the risk of diseases like e.g. diabetes, coronary heart disease and cancer. It influences life expectancy and quality of life. In studies, the influence of the microbiome on the development of overweight was evaluated. **Firmicutes** have been shown to be capable of fermenting **complex, indigestible carbohydrates** to produce short-chain fatty acids (SCFA) which are absorbed through the intestinal mucosa and

serve as additional energy sourced to the host (19, 20). Due to the fermentation of carbohydrates by firmicutes **10-12 %** more **energy** is available (21).

Bacteroidetes are not able to utilize complex carbohydrates. If firmicutes dominate bacteroides in the microbiome one speaks of an increased **firmicutes-bacteroidetes-ratio** which may promote gaining weight.

In case of patients suffering from irritable colon syndrome increased firmicutes-bacteroidetes-ratios often come along with meteorism or flatulence.

Result

The microbiome analysis showed a balanced ratio of firmicutes compared to bacteroidetes. The firmicutes-bacteroidetes-ratio is **within normal range.**

Determination of the Enterotype

Recent research showed that the human microbiome can be assigned to **three main groups-** so-called enterotypes. Intestinal bacteria develop – depending on the enterotype – stable, clearly different clusters with typical metabolic properties (9). **Enterotype 1** is characterized by high **bacteroides counts** and **enterotype 2** by strong **Prevotella** population. **Enterotype 3** is only found rarely – in hardly more than 5 % of the analysis. This type shows strong **Ruminococcus** flora.

The described enterotypes show significantly differing **metabolic performance.** The bacteroides dominated flora (enterotype 1) is optimally adjusted to the utilisation of **fat, fatty acids, protein and amino acids**. **Carbohydrates**, however, are metabolized significantly worse than by Prevotella dominated flora (enterotype 2), which in turn cannot metabolize fat and protein adequately.

The enterotypes also influence the absorption of minerals like **sodium, potassium, calcium** (11) or **iron.** Enterotypes are independent of sex or age and remain stable for years. Via **long-term change of diet** and taking **prebiotics** they can be influenced (12, 13 and positively effects human sustenance and health.

Result

The microbiome analysis indicates **enterotype 1** with dominating **bacteroides flora** and clearly less present Prevotella and Ruminococcus sp.

A bacteroides dominated flora is specialized in energy generation from **oligosaccharides**, **animal proteins** and **saturated fatty acids.** Enterotype 1 is therefore mainly only found in persons, who regularly eat meat. Bacteroides only rarely dominate in vegetarians and fruit and vegetable enthusiasts. Bacteroides species are on one hand able to **synthesize vitamins** (biotin, riboflavin (B2), pantothenic acid (B5), folic acid (B9) and vitamin C); on the other hand the enterotype also influences intestinal **nutrient absorption.** The latter is significantly lower than in Prevotella dominated enterotype 2.

Actinobacteria

Bifido bacteria are gram-positive anaerobic rod-shaped bacteria, which utilize starch, but mainly oligosaccharides. Mostly acetic and lactic acid are developed.

By developing short-chained fatty acids and related pH-value reduction in the intestinal lumen bifido bacteria do not only counteract proliferation of pathogenic bacteria (colonisation resistance), they also have anti-inflammatory effects.

Result

In case of MR. SMITH the bifido bacteria count is **within the norm.** The most common representative in the microbiome is B. adolescentis. The second common species was B. longum. A strong bifido bacteria flora protects against endogenous infections and has an anti-inflammatory effect.

Equol producing genera and species

Equol is a metabolite with strong binding affinity to estrogen receptors, which is formed by intestinal microbiota from isoflavones, ie secondary plant substances.

Recent studies suggest that the ability to bacterially produce equol from daidzin or daidzein is associated with **reduced menopausal symptoms** and a **reduced risk of chronic disease** (Birru et al., 2016; Davinelli et al., 2017; Yoshikata et al., 2016). However, the bacterial formation of Equol is strongly differing interindividually and only about 20-30% of the population of Western cultures, compared to 50-60% of Asian populations are capable of forming Equol (Setchell and Clerici, 2010).

According to recent research, almost exclusively species from the family Coriobacteriaceae from the Phylum of Actinobacteria are able to form Equol. Particularly important species are **Adlercreutzia spp.**, **Eggerthella lenta** and **Slackia spp.** (Rafii, 2015).

Result

The microbiome analysis showed a sufficient count of **equol-producing bacteria**.

Bacteroidetes

Results

Bacteroides is the most common genus in the microbiome of many people. In case of MR. SMITH 27 % are of these genus, which equals a bacteria count of 2,7 x 10^11 CFU / g Stool. Most important representa-tive in the bacteroides group is B. uniformis and B. ovatus.

Also high **prevotella** bacteria counts can be reached, especially in case of vegetarians. But here it is with 4,6 x 10^7 CFU / g stool **below normal range**.

Firmicutes

A. Development of Butyrate and Short-Chain Fatty Acids by Firmicutes

Carbohydrate fermentation in the colon leads to the development of short-chain fatty acids (SCFA) (37) and gases (H_2, CO_2, methane). SFCA detectable in stool samples are mainly **formic acid, acetic acid, propionic acid** and **butyric acid**. Dietary changes lead to altered production rates of short-chain fatty acids. **Low-carb diets** lead to butyrate development reduction to one quarter (38) while **prebiotic agents** or **increased fibre consumption** lead to butyrate and propionate increases (39), the acetate levels decrease.

Short-chain fatty acids have positive influence on health. They stimulate intestinal motility and reduce inflammatory reactions by binding with GPR receptors (GPR 41 / GPR 43).
Butyrate is the most important **energy source** for colonocytes; it has an anti-inflammatory effect (40, 41, 42), protects against cell degeneration and also has **preventive influence** in regard to colorectal carcinoma.

Propionate
is metabolized in the liver, **acetate** in peripheral tissue. It is a precursor of cholesterol metabolism and lipid development. By giving prebiotics a shift of the fermentation products – from acetate to butyrate - may therefore be an advantage and lead to reduction of the **cholesterol level** (43).

Higher **SFCA concentrations** in the intestinal tract may increase mineral consumption like for example calcium (44). Therefore alterations of the intestinal microbiota after giving **FOS** come along with an increase of calcium absorption and improvement of the bone situation.

Mainly **firmicutes** develop butyrate. Among firmicutes mostly **Eubacterium rectale**, **Roseburia species** and **Ruminococcus sp.** are potent butyrate developers. The strongest butyrate developer, however, is **Faecalibacterium prausnitzii –** also a firmicute **-** which in contrast to the other listed butyrate developers cannot utilize starch. As butyrate is quickly absorbed via the intestinal mucosa, measurements in stool only provide unreliable results. Important information about butyrate development can be obtained with the aid of quantitative analyses of butyrate developing bacteria.

Result

The molecular-genetic microbiome analysis on butyrate-forming bacteria showed **deficits in several important butyrate formers**.

The **total bacteria count** of the butyrate formers however was within the norm.

Due to deficits in several important butyrate formers, a **non-optimal butyrate formation** should be considered despite the inconspicuous total bacteria count.
E. hallii is a bacterium that can convert acetate to butyrate. The butyrate source is not available, or only to a limited extent, when the number of microorganisms is low. A butyrate deficiency can result.

Evaluation of the Clostridia Flora (Total Bacteria Count, Toxin Development)

Clostridia belong to the group of firmicutes. They are obligatory anaerobic bacteria and develop spores. Pathogens belong to the clostridia species, but also apathogenic, useful bacteria, which have an immune modulating effect and lead to an increase of IL-10. Mainly Clostridium botulinum, Clostridium tetani or Clostridium difficile belong to the group of pathogenic representatives. In regard to their favoured energy sources clostridia can be assigned to two groups: **proteolytic** and **saccharolytic species**.

Proteolytic clostridia utilize protein and amino acids. Saccharolytic species on the other hand ferment carbohydrates, starch or fibres. During this process butyrate, acetone, butanol, CO_2 and hydrogen are developed. Dominance of proteolytic species often indicates so-called **"putrescence dyspepsia",** which frequently comes along with increased pH-values in stool. If the pH-value is – in spite of high counts of proteolytic species – within the norm or reduced, this is most often caused by accelerated intestinal passage. High clostridia counts may also come along with "**fermentative dyspepsia**". In this case, however, they are saccharolytic species.

Some clostridia groups – so-called **Cluster I-Clostridia** contain **toxin developing species**, like for example C. perfringens, C. sporogenes or C. histolyticum. Cluster I clostridia are often found in diseases of the autistic spectrum disorders and are not rarely the cause of **autism associated intestinal** and frequently also **extra-intestinal complaints.**

Result

The microbiome analysis of MR. SMITH showed **increased clostridia bacteria counts**.

Toxin developing clostridia (Cluster I) could not be detected during sequencing. But only the most important representatives C. perfringens, C. sporogenes und C. histolyticum are considered.

Additional Relevant Firmicutes

Christensenella

The genus Christensenella, which was recently discovered in 2012, contains gram-negative, obligate anaerobic bacteria, which can be isolated from human feces. As extensive investigations on twins showed, the occurrence of Christensenella is to a large extent inherited. Especially twins with a **low BMI** showed high bacterial counts (Goodrich et al., 2014, Hamazelou, 2016). Animal experiments suggest that Christensenella is **counteracting obesity** (Waters et al., 2016). Christsensenella is often found in feces of very old people (Kong et al., 2016).

Result

The presence of a sufficient number of Christensenella has a positive effect, they seem to protect against overweight and its consequences and thus to promote a long life.

Dialister invisus

The Dialister species are part of the Firmicutes. Their share of the total microbiome is about **1-1.5%** (Van Zanten et al., 2014). 5 species belong to this generic group of which 3 can be determined in stool. Before all Dialister invisus is of importance – a gram-negative, obligate anaerobic bacterium – which may be involved in **oral cavity infections** (periodontitis, gingivitis) (Morio et al., 2007). Only little is known so far about the function of Dialister invisus in the intestines. They are not of physiological significance. High bacteria counts should be regarded as in indication of dysbiosis.

Result

In case of MR. SMITH the bacteria count of Dialister invisus is within normal range.

Fusobacterium spp.

In humans Fusobacteria occur as part of the physiological microbiota of the oral cavity and are regularly detected in small amounts in the intestinal microbiotia. Fusobacteria are obligatory anaerobic growing, spindle-shaped bacilli. Especially Fusobacterium nucleatum and Fusobacterium necrophorum have a pathological potential in the infectiology and in the oral cavity they are associated with caries and periodontitis.

Already in 2012, in metagenomic analysis an accumulation of Fusobacterium nucleatum in **colorectal carcinoma (CRC)** has been detected. If Fusobacteria are actually able to cause a tumour or if they use the decayed tumour tissue as “food source”, has not been clarified yet. However, an etiological relevance does not seem unlikely.

In the present case, **Fusobacterium spp. could not be detected or just in low concentration.**

Proteobacteria

Like microbiome analyses show there is decreasing digestive performance in older age, which often leads to an increase of Enterobacteriaceae (**Escherichia coli**, **Klebsiella**, **Enterobacter**, **Proteus)** or pasteurellaceae (e.g. **haemophilus**). There are also alterations of the obligatory anaerobic flora. Increases of **clostridia** are suspicious. **Bifido bacteria** and **lactobacilli** on the other hand reduce.

The described alterations can also be caused by other factors. Reapplied **antibiotic therapies** lead to increasing enterobacteria, enterococci and clostridia counts as well as to significantly decreasing bifido bacteria. (62). Similar can be observed in case of **chronic inflammatory bowel diseases or irritable colon syndromes** (63, 64).

Determination of Pathogenic or Potentially Pathogenic Bacteria

No potentially pathogenic Proteobacteria could be found in the microbiome of MR. SMITH.

Histamine-forming bacteria

In the stool sample no histamine-producing bacteria such as Hafnia alvei, Klebsiella pneumoniae or Morganella morganii could be detected.

Damage of the Intestinal Mucosa due to Hydrogen Sulphide Development (H_2S)

Hydrogen sulphide is a toxic metabolic product, which – in case of higher concentrations – leads to damage of intestinal epithelia and such promotes the occurrence of cellular atypia. H_2S is produced in the colon by **sulphate reducing bacteria** – especially by **Bilophila wadsworthii**, **Desulfomonas pigra** and **Desulfovibrio piger**. Meat is an important source of sulphur, which promotes the growth of sulphate reducing bacteria. The **cancer promoting potential** of hydrogen sulphide is based on the formation of **free radicals** (oxidative stress) and up-regulation of **cyclooxygenase-2** activity in the epithelia cells.

Gut bacteria can also produce N-nitroso compounds. Their quantity increases in case of high-protein diets, especially if a lot a meat is consumed. Cooking meat produces heterocyclic amines, which can be transformed to cancer promoting intermediate products.

Result

In the scope of sequencing no increased Bilophila wadsworthia, Desulfomonas pigra or Desulfovibrio piger counts could be determined. This indicates **minor H_2S production**.

Methanobrevibacter spp.

Methanogens such as Methanobrevibacter spp. belong to the domain of the archaea and are not bacteria. In humans, a stable colonization is found in the gastrointestinal tract and oral cavity, in the vagina and on the skin. There, methanogens form a syntropic community with other microorganisms. The most common representative in the gastrointestinal tract with >90% is Methanobrevibacter smithii.

Methanogens are able to reduce CO2 under H2 consumption, as well as secondary bacterial metabolites like acetate to methane. The frequency of methanogens is related to various diseases. Increased methanogenesis can reduce intestinal motility and promote constipation-type irritable bowel syndrome. Increased methanogenesis is also reported for Diverticulosis patients. However, by consuming H2, methanogens also favor the growth of fiber-fermenting bacteria and thus SCFA production.

In the present case, **Methanobrevibacter spp. were found only in minor bacterial counts or not at all.**

B. Oxalobacter formigenes

Oxalobacter formigenes is an oxalate decomposing anaerobic bacterium, which is often found in the colon flora. Oxalobacter formigenes lives in symbiosis with humans. If this bacterium is not or only available in insufficient counts, the primary source for the enzyme oxalyl-CoA-decarboxylase is missing. This enzyme decomposes **calcium oxalate**. Oxalyl-CoA-carbolase deficiency promotes the development **calcium oxalate containing kidney stones**.

Result

Missing evidence of **Oxalobacter formigenes** - like in case of MR. SMITH - promotes development of **calcium oxalate kidney stones.**

Bacteria with an Immunogenic Effect

E. coli and enterococci have an **immunogenic effect** and are in interaction with other bacteria mainly responsible for the **immune modulating effect of the microbiota**.
And at last **lactobacilli** together with enterococci are the main representatives of the small intestine flora. Furthermore they have an **immunogenic effect**, are **anti-inflammatory** and **stabilize the milieu.** They are able to develop substances similar to antibiotics (**bacteriocins**), which counteract proliferation of endogenic pathogens.

E.coli, enterococci and **lactobacilli** were the major pillars of intestinal flora analysis; therefore they are also taken into consideration in this context.

Result

We found reduced enterococci counts in the microbiome of MR. SMITH. Lactobacilli counts were within normal range. Low enterococci counts may indicate non-physiological flora conditions in the terminal ileum.

Mucin Development and Mucosa Barrier

In the healthy large intenstine a layer of mucosa mucus (**mucin layer**) protects the epithelial cells. If the mucin layer is damaged or insufficient mucin is formed, pathogens, pollutants or allergens can come into direct contact with the mucosa and lead to inflammation. Mucin formation and mucosal barrier are therefore closely connected. The maintenance of an intact mucosal barrier protects against bacterial translocation (LPS) and thus against inflammation. Bacteria such as **A. muciniphila** are significantly involved in maintaining the mucin layer. They emit mediator substances that stimulate the goblet cells to form mucosal mucus.

Result

The **Akkermansia muciniphila** counts in the microbiome of MR. SMITH indicate **sufficient mucin formation**.

The **Faecalibacterium prausnitzii count** in stool was **normal**.

Mycological Stool Analysis

No yeasts could be found in the stool sample of MR. SMITH.

We found **no facultative pathogenic yeasts** in the stool sample of MR. SMITH. Therefore not therapeutic measures are required.

Supplementary Parameters

Determination of Maldigestion

Digestive Capacity - Pancreas
Pancreatic elastase 1 closely correlates with the digestive capacity of the exocrine pancreas. The value determined for MR. SMITH is within **lower normal range.** Pancreas elastase values in lower normal range (between 200 and 300 ug / g) should be monitored. In these cases it is not unusual that the elastase values reduce in further and reach pathological range; patients will suffer from complaints. Therefore follow-up analysis seems sensible - especially if there are **intervals with many symptoms**.

Determination of Malabsorption

Mucosa Integrity and Permeability
The inconspicuous inflammation marker **calprotectin** indicates largely intact mucosa conditions. There are no indications of malabsorption or invasive mucosa processes.

Mucosa Immunity

Mucosa Integrity and Permeability
The increased sIgA concentration in stool indicates active defence reactions of the intestinal mucosa. This may be caused e.g. by inflammatory or allergic processes.

Helicobacter pylori – Infection of the Gastric Mucosa

Clarification of a Helicobacter Pylori Infection by Antigen Detection in Faeces

The helicobacter-pylori infection of the gastric mucosa is worldwide one of the most common infectious diseases and can be the cause of peptic ulcera or adeno carcinoma of the stomach. It can be detected in faeces with the aid of immunoassay specific antigens of helicobacter-pylori. A comprehensive European multicentre study as well as a variety of other studies have shown high sensitivity and specificity of this test before and after eradication therapy. The results were comparable to those of the 13-C urea breath test.

The lack of antigens in faeces **argues against** helicobacter-pylori infection of the gastric mucosa.

Mucosa Integrity and Detection of Colorectal Carcinoma
The inconspicuous inflammation marker **calprotectin** and **lacking evidence of micro haemorrhages** indicate intact mucosa integrity. Based on the inconspicuous values of MR. SMITH severe adenomatous polyps or colorectal carcinoma can be excluded.

In case of persisting complaints - like for example frequent abdominal pains, irregular stool, inexplicable loss of weight or visible blood deposits on stool – further clarification is definitely advisable. All people at the age of 50 should and older should have preventive medical check-ups testing calprotectin, M2PK and/ blood (haemoglobin respectively haemoglobin/haptoglobin complex) in stool once a year.

Zonulin IDK (Properdin)

Zonulin level is within **normal**.
Latest research findings lead to a reclassification of the protein measured here into **properdin** that activates the alternative complement pathway. Functionally and structurally, properdin belongs to a **"zonulin family"** of boundary surface permeability mediators that influence the t**ight junctions.**

High levels are associated with increased intestinal permeability. Low levels indicate a stable and tight intestinal mucosa. Increased intestinal permeability may induce inflammatory mucosa reactions and sensitizations. Increased values are often measured in patients with coeliac disease, diabetes mellitus type 1 or numerous other autoimmune diseases.

Therapeutic Approaches

The results of the microbiome analysis require therapeutic approaches, which protect the microflora against negative consequences or ease existing complaints by supporting the microflora.

Successful therapies, however, also take basics into consideration, which practicably apply for everyone and often already lead to significant improvement of ailments. These basic therapies are based on decade-long experiences. They are listed in short form below and can be found under www.biovis.de.

Basics for healthy intestines:

Diet	Healthy diets consist of a plentiful breakfast, a main meal at lunch and a modest dinner. It should be varied and diverse. Giving Psyllium seed husks (dosage 1-2 tablespoons) should lead to 1 – 2 formed stools per day. They are tolerated well and may also be given in case of obstipation or diarrhoea.
Wheat	Avoid or significantly reduce wheat. Wheat is often not tolerated well, even if there is no evidence of intolerance. This is caused by amylase-trypsin inhibitors (ATI), which inhibit digestive enzymes and promote mucosa irritations.
Sugar	Radical reduction of sugar consumption (maximum 1g/day)
Chewing	Thoroughly chewing and salivating of food is the first step to healthy digestion and nutrient absorption. Chewing 30-40 times leads to optimal preparation of food for intestinal processes.
Exercise	Adequate moderate exercise
Relaxation	Keep adequate resting phases
Detoxification	Drink enough (2-3 l water / unsweetened herbal teas) – this provides for improved intestinal passage and excretion of foreign matters. Possibly drainage of toxic substances via zeolite and/ or humic acids may be sensible.
Substitution	Consumption high-value herbal oils (e.g. linseed oil) and/or fish, possibly curcumin or aloe vera, which have an anti-inflammatory effect respectively promote butyrate development.

Diversity

The microbiome analysis indicates **adequate biodiversity**.

Please make sure to keep a **balanced diet** to provide for the maintenance of the microbiome diversity. An antibiotic therapy should always be accompanied by taking **probiotics.** They not only counteract proliferation of resistant pathogens, but also further reduction of bacteria diversity. Please keep in mind that also **smoking, aging, imbalanced high-fat diets** ("Western Diet") or diseases coming along with inflammatory mucosa irritations ("**low grade inflammation**") or medication (NSAR) lead to a biodiversity reduction. Therefore therapies should always start here and fight against causal factors.

Enterotype

The patient has **enterotype 1** dominated by strong bacteroides flora. Bacteroides species are able to synthesize vitamins (biotin, riboflavin, pantothenic acid, folic acid and vitamin C), but intestinal **nutrient resorption** of enterotype 1 – with the exception of some B-vitamins (B1, B2, B3) – is significantly **worse** than that of Prevotella dominated enterotype 2.

Consequence:
Enterotype 1 patients should therefore make sure their **micronutrient supply** is **adequate.** This before all applies for:

- **Vitamin A**
- **Vitamin E**
- **Iron**
- **Calcium**

Individual prebiotic or probiotic therapies

Prebiotics
Prebiotics can promote diversity and achieve targeted changes in the composition and metabolism of the gut microbiota. Prebiotics consist of hard-to-digest carbohydrates, such as **resistant starches**, which lead to the proliferation of firmicutes and some bifidobacteria. **Oligosaccharides** such as XOS, AXOS, FOS, GOS or acacia fibers also show a bifidogenic effect. They too lead to an increase in butyrate formers. In addition, Faecalibacterium prausnitzii or Akkermansia muciniphila can be propagated via FOS / GOS or acacia fibers, resulting in a stabilization of the mucus layer and the membrane barrier.

Probiotics
Probiotics are selected, living microorganisms that positively affect the environment in the intestine. Above all, strains of bifidobacteria and lactobacilli, but also E. coli, and enterococci are used. Whereas in the past it used to work predominantly with **individual strains**, it is now known that combinations of several potentiating probiotic strains can achieve significantly stronger effects. **Modern multispecies probiotics** can stimulate the mucosal immune system or have an immunomodulating effect. Depending on the selection and composition of the strains used, probiotics can stabilize the mucosal barrier in the intestine by stabilizing mast cell membranes and counteract a leaky gut. Modern multispecies probiotics have an anti-inflammatory effect and lead to a significant reduction of proinflammatory cytokines.

Pre- and probiotics should be used as specifically as possible in order to achieve an optimal effect. The selection is based on the following criteria:

• Patient age
• Complaint image
• Diversity
• Mikrobiota changes
• Butyrate and mucin formation
• Existing pathogenic / potential-pathogenic germs
• Existing facultatively pathogenic yeasts
• Inflammatory mucosal changes
• Leaky Gut (disturbed mucous membrane barrier)
• Mucosal immune system
• Incompatibilities / intolerances
• Overweight or underweight

Nutritional forms, such as **FODMAP** or **low carb** have an impact on diversity and microbiota composition. Therefore, they are also taken into account in the following compilations.

Pre- and probiotics should be used as **specifically** as possible in order to achieve an **optimal effect**. The following tables allow you to determine suitable pre- and probiotics according to fixed criteria. If prebiotics can easily be restricted to the naming of active substances, this is practically impossible with probiotics, since even the same named bacterial species can vary greatly in their abilities. Even if products are named for these reasons, a claim for completeness cannot be guaranteed due to the large number of products offered. However, attempts were made above all to include probiotics which can substantiate the indication

and efficacy with studies. If the listing is based only on similar parent compositions or indications by the manufacturer, this is marked in color. For further explanations, please refer to the tables.
MR. SMITH has a **sufficient bacterial count** of equol-producing bacteria and therefore is capable of converting soy to a relevant extent into bioactive secondary plant materials.

Equol leads to numerous positive effects, it alleviates menopausal symptoms, protects against chronic diseases, osteoporosis or complications of a metabolic syndrome.

Dietetic Treatment

The microbiome composition is significantly influenced by the diet. Long-term change of diet alters the distribution of the bacteria-phyla (e.g. of firmicutes or bacteroidetes) just like the bacteria count of bacteria species important for intestinal health.

Based on the findings the following approach seems sensible:

Dietetic Treatment

Resistant starch promotes growth of valuable butyrate developing bacteria in the intestines. At the same time the proliferation of toxin developers and putrefactive bacteria is inhibited. The following foods provide appreciable amounts of resistant starch: bananas (not too ripe), potatoes, corn products (cornflakes, tortillas etc.), cooked white beans, lentils and peas. If tolerated also bread, bread crusts or popped cereal products (e.g. cornflakes, spelt flakes, millet pops, wheat pops – best not sweetened) have positive influence.

Additional Therapeutic Approaches

Most kidney stones consist of calcium oxalate – a salt of oxalic acid. If there is an *Oxalobacter formigenes* deficiency the primary source for the enzyme oxalyl-CoA-decarboxylase is missing. This enzyme metabolizes calcium oxalate. Therefore the development of **calcium oxalate containing kidney stones** is promoted.

By **keeping low oxalate diets** one can counteract kidney stone development. Hazelnuts, almonds, amaranth, sesame, chard, spinach, rhubarb, black or green tea, mineral waters with high calcium content (more than 100 mg calcium per litre) and alcoholic drinks should be avoided. Also cocoa and wood sorrel contain a lot of oxalic acid.

With kind regards

Your Biovis-Diagnostik

Prebiotics	Butyrate formation	Anti-inflammatory	Fp and/or Am	Bifidogenic effects	F/B-Ratio	LI	FM	Flatulence*	Diversity
RS	**+**	(+)	**-**	(+)[1)]	**+**	yes	yes	**40**	**+**
PPb	**+**	**+**	**+**	**+**	**+**	yes	yes	**60**	**+**
scFOS/scGOS	**+**	**+**	**+**	**+ +**	(+)	**no**	**no**	**100**	**+**
FOS	**+**	**+**	**+**	**+**	(+)	yes	**no**	**100**	**+**
Inulin	**+**	**+**	**+**	(+)[2)]	(+)	yes	**no**	**100**	**+**
Acacia fibres	**+**	**+**	**+**	**+**	**- -**	yes	yes	**20**	**+**
XOS / AXOS	**+**	**+**	**-**	**+**	?	yes	yes	**50**	**+**
Butyrate	**+**	**+**	**-**	**-**	+/-	yes	yes	**10**	+/-
FODMAP	**-**	-	**- -**	**- -**	**- -**	yes	yes	**- -**	**- -**
Low Carb	**-**	-	+/- [3)]	+/- [3)]	**- -** [3)]	yes	yes	**- -**	**- -**

Note:

***** Relative occurrence of flatulence compared to FOS/GOS (100 %)

+ Promoting effect | **-** no detectable or only very little effect | **+/-** no influence | **- -** reduction | **yes** compatible | **not** necessarily compatible, gradually increase dosage (start: 1 g / day)

[1)] Decomposition of RS by B. breve and B. adolescentis (Aliment Pharmacol Ther 2015; 42:158-179); [2)] depending on phenotype, incomplete decomposition of inulin (Appl Environ Microbiol 2009; 75:454-461); [3)] Decreasing numbers of bacteria such as A. muciniphila (Clin Nutr Experiment 2016; 6: 39-58), F. prausnitzii- and Bifidobacteria are described with a protein- and fat-rich low-carb-diet. (Proc Nutr Soc 2015; 74: 23 – 36). Low Carb diets can contain between 25 and 250 g carbohydrates per day.

RS: Resistant Starch
PPb: „Pro Prebioma“ (combination of several prebiotic substances)
FOS/GOS: **F**ructo-/**G**alacto**o**ligo**s**accharides: short chain variants (**sc**FOS / **sc**GOS) show significantly better compatibility
XOS/AXOS: **X**ylo-, **A**rabino**x**ylo**o**ligo**s**accharides: Butyrate formation mainly through bifidogenic effect („Cross-Feeding“)
FODMAP: **F**ermentable **O**ligo-, **D**i-, **M**onosaccharides and **P**olyols“ (Polyols: polyvalent alcohols)
Fp / Am: Reproduction of Faecalibacterium prausnitzii / Akkermansia muciniphila
F/B-Ratio: Firmicutes-Bacteroidetes-Ratio
LI: Compatibility for people with lactose intolerance
FM: Compatibility for people with fructose malabsorption
Diversity: Diversity promoting effect