FlorInScan

Microbiome profile

Personalized report

LABORATOIRES RÉUNIS

Mrs.
BEE -TESTER HONEY

TESTDOKTOR
Charles TESTE
ZONE INDUSTRIELLE
LU-6131 JUNGLINSTER

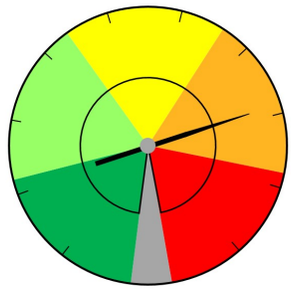
Birth date: 12.12.1986

Reference: 1803236019
Date of entry: 23.03.2018
Date of final result: 23.03.2018

Index Values

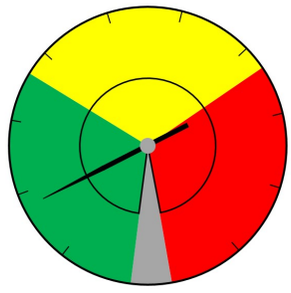
Dysbiosis index: 4

The dysbiosis index is at 4. This value points towards a pronounced dysbiosis, a dietary change is strongly recommended. The occurrence of atypical bacteria, fungi and moulds should be investigated (via FlorInScan Plus). The following index values provide further information about possible causes of the dysbiosis.



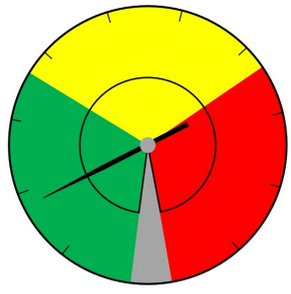
IBD index: 1

According to the IBD index of 1, the examined microbial profile does not hint towards an inflammatory bowel disease (IBD).



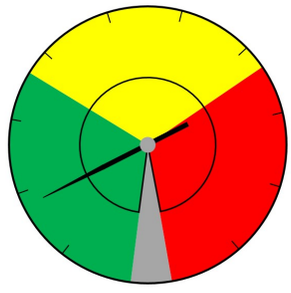
Irritable bowel syndrome (IBS) index: 1

The low IBS index of 1 indicates no abnormalities nor a predisposition pointing to an irritable bowel syndrome (IBS). However, it should be noted that some food intolerances may cause IBS even without changes in the microbial profile.



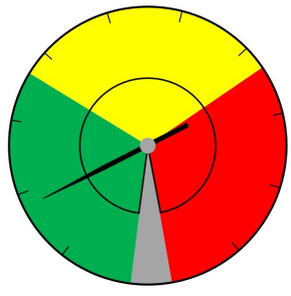
Colorectal cancer (CRC) index : 1

The CRC index is at 1. The intestinal microbiota shows no abnormalities which are indicative for CRC. Nevertheless, for patients older than 45 years, a regular preventive check-up (colonoscopy, iFOBT and/or Septin 9 test) is recommended.



Type 2 diabetes index: 1

The investigated gut microbes, which may be associated with diabetes, are in the normal range and thus inconspicuous.



Analysis	Measured value	Tolerance range

Biomarkers of a healthy gut

A. muciniphila	**0.00 %** 22.00 (13.03.2018)	0.08 - 6.50
F. prausnitzii	**2.21 %** 21.00 (13.03.2018)	2.60 - 17.00
R. bromii	**0.00 %** 36.00 (13.03.2018)	0.08 - 4.80
E. rectale	**1.79 %** 36.00 (13.03.2018)	2.30 - 15.00
E. hallii	**0.000 %** 19.000 (13.03.2018)	0.01 - 0.06
B. hydrogenotrophica	0.0001 % 12.0000 (13.03.2018)	0.0001 - 0.0100

Optional pathobionts in weakened intestinal mucosa

B. vulgatus	21.60 % 24.00 (13.03.2018)	2.75 - 24.00
B. fragilis	**0.00 %** 15.00 (13.03.2018)	0.17 - 0.93
B. ovatus	0.94 % 21.00 (13.03.2018)	0.16 - 4.00

Biomarkers for intestinal dysbiosis and low biodiversity

F. nucleatum	**0.00000 %** 25.00000 (13.03.2018)	0.00001 - 0.00030
E. faecalis	**0.0000 %** 31.0000 (13.03.2018)	0.0004 - 0.0300
A. putredinis	1.46 % 23.00 (13.03.2018)	0.04 - 3.90
R. gnavus	0.006 % 35.000 (13.03.2018)	0.003 - 0.130
R. torques	0.009 % 36.000 (13.03.2018)	0.003 - 0.290
D. formicigenerans	0.09 % 21.00 (13.03.2018)	0.04 - 0.18
C. aerofaciens	**0.02 %** 18.00 (13.03.2018)	0.04 - 0.91
H. parainfluenzae	**0.000 %** 36.000 (13.03.2018)	0.001 - 0.040
P. merdae	1.14 % 21.00 (13.03.2018)	0.50 - 3.20
C. comes	0.050 % 31.000 (13.03.2018)	0.02 - 0.09
P. copri	**0.00 %** 36.00 (13.03.2018)	0.16 - 2.90

Method: Percentage, calculated from NGS (next-generation sequencing) correlated qPCR data.

Recommendations for nutrition and nutritional supplements

Personalized nutritional advice and recommendations for specific supplements based on the measured microbiome profile for this patient are given below in tabular form. Fields highlighted in green correspond to recommendations, items with red background should be avoided or consumed only conditionally. At the end of the table information will be provided on which foods contain the recommended prebiotics.

Each bacterium is positively or negatively affected by the supply of certain nutrients. Since the colonization of certain bacteria is desired, but others should be limited in growth, a dietary recommendation is directly dependent on current bacterial colonization. Based on these complex relationships, the following individual nutritional profile was determined. For further information, the consultation of the chapter "Detailed individual consideration of individual bacteria" is recommended. Databases with detailed background information can be found here:
https://www.datapunk.net/opus23/utopia/
http://microbiomeprescription.azurewebsites.net/library/GutModifiers?mtype=FHTU.

General diet recommendations	
Based on the microbiome profile, the following diet recommendations are given:	
High fiber diet	Promotes the colonisation with a variety of useful intestinal commensals and is recommended due to the present partial deficiency.
Plant rich/vegetarien diet	A plant-rich or purely vegetarian diet can counteract an overgrowth of the putrefying flora, which is increased in the present case, and promote the growth of beneficial gut commensals.
Mediterranean diet	Mediterranean diet can positively affect the colonization with *F. prausnitzii*.
Low processed foods diet	Promotes colonization with mucosaprotective commensals.
Ketogenic diet	Promotes *A. muciniphila*, but should only be done under medical supervision due to the risk of vitamin imbalance.
Fasting	Fasting can favor the colonization with useful strains (*A. muciniphila* & *F. prausnitzii*).

Based on the microbiome profile, the following diets should be avoided:	
High fat diet	Due to the presence of a decreased mucosal protective flora, an increased presence of putrefactive bacteria and / or colorectal cancer biomarkers, a high fat diet should be avoided.
High red meat diet	Due to the partial lack of beneficial species, an increase in potentially harmful strains (*Bacteroides*) for the intestinal mucosa and / or putrefactive bacteria, red meat intake should be reduced or avoided.
High animal protein diet	Due to a decreased level of the protective flora and / or the presence of putrefactive bacteria, plant proteins should be preferred to those of animal origin.

Prebiotics	
Inulin	Promotes the colonization with a variety of beneficial commensal bacteria, including mucosa-protective species. Dose guideline: 10 g/day (www.webmd.com). Inulin is recommended because of the existing partial lack of beneficial intestinal flora.
Pectin	Promotes the colonization with *F. prausnitzii*.
XOS (xylo-oligosaccharide)	Dosage Guideline: 1-5 g/day. Available in the form of dietary supplements (www.sciencedirect.com).
Beta-glucans	Protects against potential mucosa-damaging intestinal flora (*Bacteroides*) and promotes colonisation with *R. bromii*. Dosage (glucan from barley): 3-10 g / day (www.webmd.com).
Arabinogalactan (arabic gum)	Promotes the colonisation with *A. muciniphila* und *F. prausnitzii*. Included in larch preparations.
Arabinoxylan oligosaccharide	Promotes the colonization with *A. muciniphila*. Contained in rye and supplement preparations.

Vitamins and supplements	
Due to the present microbiome profile, supplementation with the following vitamins and supplements should be considered:	
Vitamin B9 (Folate)	
Vitamin B2 (Riboflavin)	

On the basis of the determined microbiome profile, the following supplements can not or only conditionally be recommended:	
Omega-3 fatty acids	A possible supplementation should be reduced or terminated in the presence of a normal omega-3 index.

Sugars and substitutes	
Based on the microbiome profile, the following sweeteners should be used:	
Galactose (milk sugar)	As a dietary supplement and sugar replacement. Promotes colonisation with *F. prausnitzii.*
Stachyose (soy oligosaccharide)	In moderate quantities beneficial for the colonisation with *F. prausnitzii*, can cause meteorism.
Sucralose	Use as a sugar substitute, promotes *F. prausnitzii* colonization and can reduce high *Bacteroides* levels. Daily dose up to 15 mg/kg, corresponding to approx. 1 g/day.

Based on the microbiome profile, the following sweeteners should be avoided:	
Raffinose	Especially in legumes and sugar beets, it is not recommended due to reduced *F. prausnitzii* and/or increased *B. fragilis*.

Various foods

Cranberries	Contains polyphenols
Black rasberries	Contains polyphenols
Rhubarb	Contains polyphenols
Green tea	Contains polyphenols
Pomegranate	Contains polyphenols
Red wine	May have a positive effect on the intestinal flora in moderate quantities due to its polyphenol content, but excessive and habitual consumption should be avoided!
Black beans, navy beans	Promotes the colonisation with *R. bromii*.
Cruciferous vegetables (broccoli, cabbage)	Promotes the colonisation with *E. rectale* and *E. hallii*.
Apple	Contains pectin, inulin, FOS. Promotes *F. prausnitzii*, against *F. nucleatum*.

Information concerning drugs and substances which may have adverse effects on the microbiome composition	
Acetylsalicylic acid/Aspirine	May adversely affect *A. muciniphila* levels.
Resveratrol	A possible intake should be reduced; a regular red wine consumption should be limited.

The following table provides additional information on the nutritional recommendations.

Information about nutritonal recommendations	
Inulin	A starchy dietary fiber (fructans) found in a wide variety of fruits, vegetables, and herbs, including wheat, onions, bananas, leeks, artichokes, and asparagus. The inulin that is used as prebiotic is most commonly obtained by soaking chicory roots in hot water.
Pectin	Pectin is found in a variety of relatively tight/hard fruits and vegetables, especially apples, oranges, apricots, cherries and carrots.
Beta-glucans	Beta-glucans are fibers that are naturally found in the cell walls of fungi (edible mushrooms and yeasts) and plants. Wholegrain cereals contain many beta-glucans, especially oats, barley and rye. In contrast, wheat is only an average beta-glucan supplier.

Recommended Tests

Additional information on recommended medical tests can be found in the following table.

Recommendations for additional tests/diagnostic biomarkers	
Metabolic syndrome, lipid metabolism disorders	Total cholesterol, HDL, LDL, triglycerides, fasting glucose.
Type II diabetes	HOMA-index, HbA1c.
IBD (inflammatory bowel diseases)	Inflammation, local immune response and intestinal permeability: calprotectin, secretory IgA, alpha-1-antitrypsin (**FlorInScan Plus**), ultrasensitive CRP, anti-pANCA, ASCA.
CRC	iFOBT: immunological fecal occult blood testing (>55 years of age), included in the **FlorInScan plus**.

Interpretation of individual biomarkers

This chapter shows, sorted by categories, the possible deviations of their intestinal flora from the norm. It should be noted that individual deviations usually have no medical significance, since the composition of their intestinal flora can be subject to individual and temporal variations. However, attention should be paid to the increased occurrence of indicative markers for certain intestinal diseases.

I - Biomarkers of a healthy gut

Biomarkers of a healthy intestine constitute an important indicator for the nutrient supply of the intestinal epithelium (in particular butyrate producers like *F. prausnitzii*, *E. rectale*, and *E. hallii*), an intact and functional intestinal mucosa (*A. muciniphila*) and stand for high biodiversity of the intestinal flora.

The relative abundance of ***A. muciniphila*** is decreased. Possible associations: metabolic syndrome, lipid metabolism disorder, glucose intolerance, prediabetes, T2D or IBD (UC and CD).
- *Dietary recommendations:* Increased uptake of cranberry extract, grape juice, red wine, rhubarb, green tea and avoid processed foods. Weight reduction and reduced caloric uptake if overweight.
- *Recommendation(s) for additional diagnostic testing depending on the clinical manifestations or suspicion:* Metabolic syndrome, type 2 diabetes, IBD.

The relative abundance of ***F. prausnitzii*** is decreased. Possible associations: intestinal inflammatory status, metabolic syndrome, lipid metabolism disorder, glucose intolerance, prediabetes, T2D, IBD (UC and CD) and CRC.
- *Dietary recommendations:* Increased uptake of raffinose (found in beans, cabbage, brussels sprouts, broccoli, asparagus, other vegetables, and whole grains), inulin (see below), vitamin B12 (milk, eggs, malted barley, liver, kidney, heart, leafy vegetables & yeast). In general, a “plant-based diet” rich in grains, legumes, fruits, and vegetables should be preferred.
- *Recommendation(s) for additional diagnostic testing depending on the clinical manifestations or suspicion:* T2D, Metabolic syndrome & lipid metabolism disorders, IBD, CRC, butyrate production (fecal short chain fatty acids (SCFAs) analysis).

The relative abundance of ***R. bromii*** is decreased. Possible associations are intestinal inflammatory status or IBD (UC and CD).
- *Dietary recommendations*: Increased uptake of resistant starch (type II), whole-grain barley and black beans. Prefer a “plant-based diet” rich in grains, legumes, fruits, and vegetables.
- *Recommendation(s) for additional diagnostic testing depending on the clinical manifestations or suspicion:* IBD; Fecal short chain fatty acids (SCFAs) analysis.

The relative abundance of ***E. rectale*** is decreased. Possible associations: intestinal inflammatory status, IBD (UC and CD) and CRC.
- *Dietary Recommendations:* Increased uptake of red wine (with moderation), whole-grain barley, black beans and especially of type II resistant starch (see below).
- *Recommendation(s) for additional diagnostic testing depending on the clinical manifestations or suspicion:* IBD, fecal short chain fatty acids (SCFAs).

The relative abundance of ***E. hallii*** is decreased. Possible associations: intestinal inflammatory status, IBD (CD).
- *Dietary Recommendations:* Increased uptake of dietary fibers (fruits, vegetables, legumes, whole grains, nuts and seeds).
- *Recommendation(s) for additional diagnostic testing depending on the clinical manifestations or suspicion:* IBD.

II - Facultative pathobionts in weakened intestinal mucosa

These organisms are part of the normal intestinal flora but may cause clinical manifestations and promote inflammatory processes, especially in the case of a weakened intestinal mucosa (and a lack of Group I organisms, above).

All biomarkers of this category show an uncritical level of abundance.

The relative abundance of ***B. fragilis*** is decreased. In most cases, this finding has no clinical relevance. A possible association exists with Parkinson disease.
- *Dietary Recommendations:* A diet containing considerable amounts of meat, moderate amounts of red wine and Fructo-oligosaccharides (FOS, see below) can help to normalize the level.

III – Biomarkers for intestinal dysbiosis and low biodiversity

Most of the bacteria of group III are found as part of the normal intestinal flora even in the healthy intestine. However, an increased abundance tends to be associated with intestinal problems and diseases. Many of these species are inflammatory in case of excessive colonization, attack the intestinal mucosa (*R. gnavus*, *R. torques*) or can cause meteorism (*D. formicigenerans*). Even though they represent gut commensals, particular attention should be given to a subtantially increased number of *F. nucleatum* and *E. faecalis*. These preferentially colonize cancerous tissue, on the other hand their increased presence can also be due to high-fat diet. The latter as well as meat consumption also promote putrefying flora (*A. putredinis*).

All biomarkers of this category show an uncritical level of abundance.

The relative abundance of ***E. faecalis*** is decreased or it is absent. This may lead toadeficiency of the acidifying flora.

The relative abundance of ***F. nucleatum*** is decreased or it is absent. This finding is without any clinical significance.

The relative abundance of ***H. parainfluenza*** is decreased. This finding is normally without any clinical significance.

The relative abundance of ***P. copri*** is decreased. This finding is normally without any clinical significance.

The relative abundance of ***C. aerofaciens*** is decreased. Normally without any clinical significance, this result may be associated with IBS.

Explanations

Fequently used abreviations:

UC: ulcerative colitis
CD: Crohn's disease
T2D: Typ 2 diabetes
IBD: inflammatory bowel disease
CRC: colorectal carcinoma
SCFAs: short fatty acids
IBS: Irritable bowel syndrome

Akkermansia muciniphila

A. muciniphila, a common inhabitant of the human intestine, accounting for 1–4% of the overall colon microbiota[1] , is a mucin-degrader involved in a regular balanced process of self-renewing intestine[2] maintaining the mucin layer thickness. Through an increase in gut integrity[3-5], *A. muciniphila* contributes to maintain gut health[6-8], improves glucose homeostasis[9] and decreases metabolic endotoxemia[5].
Enrichment of *Akkermansia* following dietary modification frequently coincides with improved metabolic parameters. A decline in *A. muciniphila* in the colon correlates with several diseases, such as obesity, type 2 diabetes (T2D), and inflammatory bowel disease (IBD) both Crohn's Disease (CD) and ulcerative colitis (UC)[6,7,10,11], whereas an excessive abundance of *Akkermansia* has been observed in Parkinson's disease patients[12]. Important variations of *A. muciniphila* quantity may be observed in the intestine of obese/overweight subjects. A recent human study shows that below a given fecal amount obese/overweight subjects were less disposed to respond to the beneficial effect of a caloric restriction diet in terms of improved cardio-metabolic risk factors (i.e. plasma cholesterol, inflammation, insulin resistance and glycemia)[13].

Faecalibacterium prausnitzii

Faecalibacterium prausnitzii, one of the most abundant butyrate-producing bacterium in the gut[14], accounts for 5 to 15 % of the total faecal microbiome in healthy adults[15]. It has a mucosal protective role through its important anti-inflammatory activity[16-18] and plays a crucial role in maintaining gut physiology and host well-being. Its high relative abundance is associated with a greater bacterial gene richness in the gut[19] and it could serve as an indicator or biomarker of intestinal health in adults[20]. *F. prausnitzii* can be considered as a promising probiotic candidate for the treatment of pathologies characterized by chronic gut inflammation as well as for the protection against glucose intolerance and type 2 diabetes[21,22]. The presence of *F. prausnitzii* has been correlated with a protection of patients against IBD and a higher proportion of this bacterium in the gut microbiome tends to be associated with disease remission[23]. A decrease in abundance in *F. prausnitzii* is associated with the onset of inflammatory status and has been extensively described in several intestinal inflammatory disorders like CD and UC[24-28] as well as in CRC[29].

Ruminococcus bromii

Ruminococcus bromii is a keystone species for the degradation of resistant starch (RS) in the human colon and for the production of butyrate and other short chain fatty acids (SCFAs)[30,31]. Introduction of RS in the diet increases the abundance of *R. bromii* and has a wide range of health-promoting effects suggesting the importance of the metabolic activity of *R. bromii* for the wellbeing of the host[32,33]. A decrease in the abundance of *R. bromii* is observed in Crohn's disease[34,35] and ulcerative colitis patients[36].

Eubacterium rectale

Eubacterium rectale, a core member of the human healthy gut microbiota that is responsible for butyrate formation[31], mainly through carbohydrate fermentation. This is an important trait, as butyrate is the preferred energy source for colonocytes and has a protective effect against colon diseases. *E. rectale* cannot directly utilize resistant starch (RS). Thus, *Ruminococcus bromii* is required to begin the initial degradation of the RS granules, liberating metabolites that *E. rectale* can utilize to produce butyrate[30]. Because of this cross-feeding, *E. rectale* increases with *R. bromii* when the host consumes a diet rich in RS[37]. A decrease in abundance is observed in CD[38], UC[36] and CRC[29].

Eubacterium hallii

With its ability to use a broad range of substrates, *E. hallii* is a key species within the intestinal trophic chain with the potential to highly impact the metabolic balance as well as the gut microbiota/host homeostasis by the formation of different short chain fatty acids and reuterin, a metabolite with antimicrobial properties[39]. Moreover, based on its ability to utilize lactate, *E. hallii* is considered an important microbe with regard to intestinal metabolic balance as lactate accumulation has been associated with several intestinal diseases[39]. A decrease in abundance is observed in Crohn's disease[40].

Blautia hydrogenotrophica

Blautia hydrogenotrophica is an important trophic member of the gut ecosystem due to its capacity to utilize colonic gas for the production of acetate that is rerouted in butyrate by the butyrogenic species. It plays an important role in both gas reduction and butyrate production in the colon[41,42]. A decrease in relative abundance of *B. hydrogenotrophica* could be associated with an increased volume of fermentation gases (H_2 and CO_2) as well as abdominal bloating and pain in patients with irritable bowel syndrome (IBS)[43]. A decrease in abundance has been observed in pre-diabetic subjects[44].

Bacteroides

Bacteroides is a predominant genus of anaerobic bacteria making up ~25% of the total gut microbiome[45]. *Bacteroides* species, normal commensals of the GI tract, are generally beneficial to human health via their production of polysaccharides, volatile fatty acids, cleavage of dietary fibers into digestible short-chain fatty acids, and other nutrients. However, when they escape this environment they can cause substantial inflammatory pathology with significant morbidity and mortality[46]. Amongst the *Bacteroides* genus, different species (*B. vulgatus*, B. *fragilis*, *B. ovatus* and others) might become pathobiont depending on microbiota composition, availability of certain nutrients and gut permeability. Species such as *B. fragilis* and *B. vulgatus* are implicated in the disruption of the intestinal barrier integrity, thereby contributing to the development of inflammation[47]. Those species have an invasive effect on the host enteric tissue and can cause a systemic antibody response[48].

Bacteroides vulgatus

The pathobiont *B. vulgatus* has been reported to produce mucin-degrading enzymes, which could profoundly affect mucosal barrier functions[49]. As *B. fragilis, Bacteroides vulgatus* is thought to be responsible for the exaggeration of inflammation and immune response in inflammatory bowel disease (IBD)[50-53] and has been implicated in the etiology of both Crohn's disease and ulcerative colitis[50,51]. For example, an elevation in the level of serum antibody to *B. vulgatus* has been demonstrated in ulcerative colitis[51]. CD[54] as well as UC[55] and CRC[56,57] individuals have been shown to have a higher relative abundance of *B. vulgatus*. In association with *Prevotella copri, B. vulgatus* could be an intestinal microbial signature linked to type 2 diabetes development[58]. Lower levels of *B. vulgatus* have been seen in IBS patients in comparison to healthy controls[59]. In contrast, significant higher numbers can be found in stool of severe autistic children when compared to controls[60].

Bacteroides fragilis

Bacteroides fragilis, even if it colonizes most humans, is not the most prevalent anaerobic species in the intestinal tract (accounting for 0.5% of the normal human colonic flora) but is regarded as the most virulent species and has been implicated in various infections such as intra-abdominal sepsis, deep-seated abscesses, and necrotizing skin and soft tissue infections[61]. There are 2 classes of *B. fragilis* distinguished by their ability to secrete a zinc-dependent metalloprotease toxin, *B. fragilis* toxin (BFT). Strains that do not secrete BFT are non-toxigenic *B. fragilis* (NTBF), and those that do are called enterotoxigenic *B. fragilis* (ETBF). ETBF can induce clinically manifesting pathologies, including inflammatory diarrhea, although asymptomatic colonization may be common[62]. The BFT has a proteolytic activity which is responsible for the degradation of tight junction proteins[63] and therefore leads to a dysfunction of the intestinal epithelial barrier with enhanced epithelial permeability and damaged intestinal crypts and colonocytes[64,65]. A high abundance in *B. fragilis* is observed in acute diarrhea[66], IBD (active state of CD)[67], and CRC[68-71]. Moreover, increased levels have been proven in children with chronic functional constipation[72]. *In Celiac Disease, B. fragilis* is more frequently identified in patients than in healthy

controls[47]. In Parkinson Disease, patients have less B. *fragilis* than healthy people[73,74].

Bacteroides ovatus

Bacteroides ovatus is a common human gut bacterium capable of degrading several complex plant cell wall polysaccharides[75,76] and is considered as a general fecal contamination indicator[77]. It is one of the most predominant commensal intestinal microbes causing a systemic antibody response in inflammatory bowel disease[78]. *B. ovatus* is so highly antigenic that it surpasses the anti-inflammatory regulation exerted by an IgA response and thus can also cause an inflammatory IgG response[78]. CD individuals have been shown to have a higher relative abundance of *B. ovatus*[54]. *Bacteroides ovatus* has been shown to be increased in children with chronic functional constipation[72]. Furthermore, high levels of *B. ovatus* correlate with the development of T1D-associated autoimmunity in young children who are at high genetic risk for this disorder[79]. However, decreased levels of *B. ovatus* were associated with irritable bowel syndrome[59].

Ruminococcus gnavus

Ruminococcus gnavus is a mucin-degrading and non-butyrate producing bacterium[80] present in 90% of individuals[81] and has been implicated in gut-related diseases such as IBD[6]. Increased numbers of *R. gnavus* boost the mucosal barrier degradation and enhance bacterial translocation leading to an increase in gut permeability[82]. Among *Firmicutes*, *R. gnavus* appears to be particularly over-represented in CD patients[83,84] and is increased in macroscopically and histologically normal intestinal epithelium of both CD and UC patients[6,80]. The numbers of *R. gnavus* has also been shown to be higher in T2D patients compared to healthy individuals[85]. An increased fecal abundance was associated with the onset of allergic diseases in infants as they cause inflammation in the intestinal tract. Subsequently, it increases the number of lymphocytes and eosinophils that are released into blood and lymphatic circulation, and in turn causes an allergic reaction in the respiratory tract[86].

Ruminococcus torques

Ruminococcus torques is a mucin-degrading[87] bacterium of the mucosa layer in the colon and a non-butyrate producing bacteria showing increased numbers in the mucosa of adults with IBD[86,88]. This bacterium has pro-inflammatory properties, due to the expression of certain proteins that are recognized by specific components of the humoral immune system[89,90]. An increased abundance of *R. torques* can be observed in IBS patients and is positively correlated with IBS symptoms[91]. Moreover, increased levels are observed in feces of children with autism spectrum disorder (ASD); in particular if associated with reported functional gastrointestinal disorder than those without such a disorder[92].

Enterococcus faecalis

E. faecalis, abundant commensal bacterial species in the human gut microbiome displays a dualistic character as it can contribute to the development of intestinal inflammation through mechanisms that impair epithelial barrier functions and is known to play a role in a number of infectious processes such as endocarditis, bacteremia, and urinary tract infections[93]. Increased *E. faecalis* is a prominent feature in patients with IBD, especially Crohn's disease where a significant augmentation appears to be associated with clinically active status[94]. In addition to its ability to induce chronic inflammation, *E. faecalis* was shown to produce extracellular superoxide and hydrogen peroxide[95] able to induce DNA damage[96]. *E. faecalis* has been found to be enriched in faecal samples from CRC patients compared to healthy individuals[29] as well as in tumors and adjacent tissues of CRC patients compared to mucosa from healthy individuals[97].

Fusobacterium nucleatum

F. nucleatum, a strictly anaerobic oral commensal and periodontal pathogen, is implicated in gastrointestinal disorders such as appendicitis[8,98], irritable bowel disease and colorectal cancer. It has been detected in colonic biopsies of patients with IBD[99,100] suggesting a causal relevance for the disease. Moreover, it has been associated with CRC[101-103] as its prevalence is enhanced in mucosa from patients with CRC compared to control subjects[104] and is found in a higher proportion in CRC tumors compared to adjacent normal tissue[105,106]. Different studies report that levels of *F. nucleatum* are elevated in adenomas, in stools of patients with adenoma and carcinoma, and are associated with colorectal neoplasia[107-111].

Dorea formicigenerans

Dorea formicigenerans, a major gas producing bacterium in the human intestine[112], was reported to be significantly increased in abundance in paediatric and adult IBS patients[91,113]. *Dorea* species is a mucosa-associated bacterium implicated in mucin degradation via its ability to metabolize sialic acids which are commonly found at terminal ends of mucins. The release of these acids potentially increases gut permeability[114]. Members of the *Dorea* genus have also been found in greater abundance in patients with ulcerative colitis[115].

Haemophilus parainfluenzae

The *Haemophilus* species found in the gastrointestinal tract originates from the oropharynx and saliva[116]. The microbiomes of children with irritable bowel syndrome are characterized by a significantly greater percentage of *Haemophilus parainfluenzae*[113]. Proportions of *H. parainfluenzae* were shown to be significantly higher in feces from carcinoma and adenoma patients than in those from control subjects where this bacterium was barely detectable[117].

Prevotella copri

Prevotella strains are classically considered commensal bacteria due to their extensive presence in the healthy human body and are linked to vegetarism in Western populations[118-120]. However, emerging studies have linked increased *Prevotella* abundance to inflammatory disorders, suggesting that at least some strains exhibit pathobiontic properties[121]. *Prevotella* are mucin degrading bacteria, which may be associated with increased gut permeability and may therefore be related to low-grade inflammation, which is detrimental with respect to metabolism[122]. In association with *B. vulgatus, P. copri* could be an intestinal microbial signature linked to type 2 diabetes development[58] and high levels of *P. copri* are shown to induce insulin resistance[123]. *Prevotella copri* is strongly correlated with disease in new-onset of untreated rheumatoid arthritis (NORA) patients. *P. copri* colonization increases the risk of rheumatoid arthritis from 1% to 3.95%[124].

Collinsella aerofaciens

Collinsella aerofaciens, the most abundant actinobacterium in the healthy gastrointestinal tract is the major utilizer of lactose in the human colon[125]. An altered abundance of *C. aerofaciens* may be linked with several health disorders like IBS, IBD, type 2 diabetes and atherosclerosis. *C. aerofaciens* shows a significant decrease in all IBS subtypes compared with healthy controls[126]. Patients with IBD have more *Collinsella aerofaciens* than healthy subjects[83]. A higher abundance of the genus *Collinsella* is observed in T2D[127,128] and CRC[107] patients compared to controls. This genus shows statistically significant and positive correlations to total and LDL cholesterol[129], and is also enriched in patients with symptomatic atherosclerosis defined as stenotic atherosclerotic plaques in the carotid artery leading to cerebrovascular events[130].

Parabacteroides merdae

Parabacteroides merdae is part of normal human gut flora but have been shown to be enriched in carcinomas[131] and frequently distributed in hypertensive gut microbiome[132].

Alistipes putredinis

Alistipes are commensal to the gut and, in limited quantities, are indicative of gastro-intestinal good-health. However, these microbes, composed of putrefactive bile-tolerant anaerobes, increase with consumption of high-fat animal-based proteins[133] and have been associated with different pathologies. *A. putredinis* has been isolated from intestinal tissues in cases of appendicitis in children[134,135]. In pediatric IBS patients, *Alistipes putredinis* has been associated with the phenotype of frequently recurrent abdominal pain[113]. It is also enriched in carcinoma samples compared with both healthy and advanced adenoma samples[131]. An increased abundance of *Alistipes putredinis* is observed in obesity[136] and a positive association was described with T2D in humans[137]. It might be a bacterial genus of interest in the field of obesity as it was more abundant at baseline in participants successful in losing and maintaining their weight during and after a weight-loss intervention[136]. *Alistipes* influence the availability of tryptophan, a precursor of serotonin and an enrichment has been observed in depressed subjects[138].

Coprococcus comes

Coprococcus comes which has been identified as a 'core species' of the human healthy gut microbiome is a butyrate-producing species mainly through carbohydrate fermentation. The relative abundance of *Coprococcus comes* has been shown to increase in inflammatory bowel disease patients[139].A possible role for *C. comes* in the pathogenesis of CD has been suggested based on its interaction with the immune system[140]. It can activate complement and thereby induce inflammation. Moreover, these bacteria are not ingested by neutrophils and can bind immunoglobulins through their Fc region which prevents phagocytosis of this microorganism[140].

References

1 Derrien, M. *et al.* The Mucin degrader Akkermansia muciniphila is an abundant resident of the human intestinal tract. *Appl Environ Microbiol* 74, 1646-1648, doi:10.1128/AEM.01226-07 (2008).
2 Salminen, C. G. G. S. Novel Probiotics and Prebiotics: How Can They Help in Human Gut Microbiota Dysbiosis? *Applied food biotechnology* 3, 72-81, doi:http://dx.doi.org/10.22037/afb.v3i2.11276 (2016).
3 Shin, N. R. *et al.* An increase in the Akkermansia spp. population induced by metformin treatment improves glucose homeostasis in diet-induced obese mice. *Gut* 63, 727-735, doi:10.1136/gutjnl-2012-303839 (2014).
4 Anhe, F. F. *et al.* A polyphenol-rich cranberry extract protects from diet-induced obesity, insulin resistance and intestinal inflammation in association with increased Akkermansia spp. population in the gut microbiota of mice. *Gut* 64, 872-883, doi:10.1136/gutjnl-2014-307142 (2015).
5 Everard, A. *et al.* Cross-talk between Akkermansia muciniphila and intestinal epithelium controls diet-induced obesity. *Proc Natl Acad Sci U S A* 110, 9066-9071, doi:10.1073/pnas.1219451110 (2013).
6 Png, C. W. *et al.* Mucolytic bacteria with increased prevalence in IBD mucosa augment in vitro utilization of mucin by other bacteria. *Am J Gastroenterol* 105, 2420-2428, doi:10.1038/ajg.2010.281 (2010).
7 Vigsnaes, L. K. *et al.* Gram-negative bacteria account for main differences between faecal microbiota from patients with ulcerative colitis and healthy controls. *Benef Microbes* 3, 287-297, doi:10.3920/BM2012.0018 (2012).
8 Swidsinski, A. *et al.* Acute appendicitis is characterised by local invasion with Fusobacterium nucleatum/necrophorum. *Gut* 60, 34-40, doi:10.1136/gut.2009.191320 (2011).
9 Joyce, S. A. & Gahan, C. G. The gut microbiota and the metabolic health of the host. *Curr Opin Gastroenterol* 30, 120-127, doi:10.1097/MOG.0000000000000039 (2014).
10 Cani, P. D. & Everard, A. [Akkermansia muciniphila: a novel target controlling obesity, type 2 diabetes and inflammation?]. *Med Sci (Paris)* 30, 125-127, doi:10.1051/medsci/20143002003 (2014).
11 Schneeberger, M. *et al.* Akkermansia muciniphila inversely correlates with the onset of inflammation, altered adipose tissue metabolism and metabolic disorders during obesity in mice. *Sci Rep* 5, 16643, doi:10.1038/srep16643 (2015).
12 Heintz-Buschart, A. *et al.* The nasal and gut microbiome in Parkinson's disease and idiopathic rapid eye movement sleep behavior disorder. *Mov Disord* 33, 88-98, doi:10.1002/mds.27105 (2018).
13 Dao, M. C. *et al.* Akkermansia muciniphila and improved metabolic health during a dietary intervention in obesity: relationship with gut microbiome richness and ecology. *Gut* 65, 426-436, doi:10.1136/gutjnl-2014-308778 (2016).
14 Flint, H. J. *et al.* Microbial degradation of complex carbohydrates in the gut. *Gut Microbes* 3, 289-306, doi:10.4161/gmic.19897 (2012).
15 Hold, G. L. *et al.* Oligonucleotide probes that detect quantitatively significant groups of butyrate-producing bacteria in human feces. *Appl Environ Microbiol* 69, 4320-4324 (2003).
16 Sokol, H. *et al.* Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc Natl Acad Sci U S A* 105, 16731-16736, doi:10.1073/pnas.0804812105 (2008).
17 Miquel, S. *et al.* Identification of metabolic signatures linked to anti-inflammatory effects of Faecalibacterium prausnitzii. *MBio* 6, doi:10.1128/mBio.00300-15 (2015).
18 Lopez-Siles, M. *et al.* Faecalibacterium prausnitzii: from microbiology to diagnostics and prognostics. *ISME J* 11, 841-852, doi:10.1038/ismej.2016.176 (2017).
19 Le Chatelier, E. *et al.* Richness of human gut microbiome correlates with metabolic markers. *Nature* 500, 541-546, doi:10.1038/nature12506 (2013).
20 Miquel, S. *et al.* Faecalibacterium prausnitzii and human intestinal health. *Curr Opin Microbiol* 16, 255-261, doi:10.1016/j.mib.2013.06.003 (2013).
21 Martin, R. *et al.* Functional Characterization of Novel Faecalibacterium prausnitzii Strains Isolated from Healthy Volunteers: A Step Forward in the Use of F. prausnitzii as a Next-Generation Probiotic. *Front Microbiol* 8, 1226, doi:10.3389/fmicb.2017.01226 (2017).
22 El Hage, R. *et al.* Emerging Trends in "Smart Probiotics": Functional Consideration for the Development of Novel Health and Industrial Applications. *Front Microbiol* 8, 1889, doi:10.3389/fmicb.2017.01889 (2017).
23 Wong, C., Harris, P. J. & Ferguson, L. R. Potential Benefits of Dietary Fibre Intervention in Inflammatory Bowel Disease. *Int J Mol Sci* 17, doi:10.3390/ijms17060919 (2016).
24 Sokol, H. *et al.* Low counts of Faecalibacterium prausnitzii in colitis microbiota. *Inflamm Bowel Dis* 15, 1183-1189, doi:10.1002/ibd.20903 (2009).
25 Lopez-Siles, M. *et al.* Changes in the Abundance of Faecalibacterium prausnitzii Phylogroups I and II in the Intestinal Mucosa of Inflammatory Bowel Disease and Patients with Colorectal Cancer. *Inflamm Bowel Dis* 22, 28-41, doi:10.1097/MIB.0000000000000590 (2016).
26 Lopez-Siles, M. *et al.* Mucosa-associated Faecalibacterium prausnitzii phylotype richness is reduced in patients with inflammatory bowel disease. *Appl Environ Microbiol* 81, 7582-7592, doi:10.1128/AEM.02006-15 (2015).
27 Jia, W. *et al.* Is the abundance of Faecalibacterium prausnitzii relevant to Crohn's disease? *FEMS Microbiol Lett* 310, 138-144, doi:10.1111/j.1574-6968.2010.02057.x (2010).
28 Machiels, K. *et al.* A decrease of the butyrate-producing species Roseburia hominis and Faecalibacterium prausnitzii defines dysbiosis in patients with ulcerative colitis. *Gut* 63, 1275-1283, doi:10.1136/gutjnl-2013-304833 (2014).
29Balamurugan, R. *et al.* Real-time polymerase chain reaction quantification of specific butyrate-producing bacteria, Desulfovibrio and Enterococcus faecalis in the feces of patients with colorectal cancer. *J Gastroenterol Hepatol* 23, 1298-1303, doi:10.1111/j.1440-1746.2008.05490.x (2008).
30 Ze, X. *et al.* Ruminococcus bromii is a keystone species for the degradation of resistant starch in the human colon. *ISME J* 6, 1535-1543, doi:10.1038/ismej.2012.4 (2012).
31 Morrison, D. J. & Preston, T. Formation of short chain fatty acids by the gut microbiota and their impact on human metabolism. *Gut Microbes* 7, 189-200, doi:10.1080/19490976.2015.1134082 (2016).
32 Walker, A. W. *et al.* Dominant and diet-responsive groups of bacteria within the human colonic microbiota. *ISME J* 5, 220-230, doi:10.1038/ismej.2010.118 (2011).
33 Abell, G. C. *et al.* Phylotypes related to Ruminococcus bromii are abundant in the large bowel of humans and increase in response to a diet high in resistant starch. *FEMS Microbiol Ecol* 66, 505-515, doi:10.1111/j.1574-6941.2008.00527.x (2008).
34 Nagao-Kitamoto, H. & Kamada, N. Host-microbial Cross-talk in Inflammatory Bowel Disease. *Immune Netw* 17, 1-12, doi:10.4110/in.2017.17.1.1 (2017).
35 Kang, S. *et al.* Dysbiosis of fecal microbiota in Crohn's disease patients as revealed by a custom phylogenetic microarray. *Inflamm Bowel Dis* 16, 2034-2042, doi:10.1002/ibd.21319 (2010).
36 Rajilic-Stojanovic, M. *et al.* Phylogenetic analysis of dysbiosis in ulcerative colitis during remission. *Inflamm Bowel Dis* 19, 481-488, doi:10.1097/MIB.0b013e31827fec6d (2013).
37 Cockburn, D. W. *et al.* Molecular details of a starch utilization pathway in the human gut symbiont Eubacterium rectale. *Mol Microbiol* 95, 209-230, doi:10.1111/mmi.12859 (2015).
38 Man, S. M., Kaakoush, N. O. & Mitchell, H. M. The role of bacteria and pattern-recognition receptors in Crohn's disease. *Nat Rev Gastroenterol Hepatol* 8, 152-168, doi:10.1038/nrgastro.2011.3 (2011).
39 Engels, C. *et al.* The Common Gut Microbe Eubacterium hallii also Contributes to Intestinal Propionate Formation. *Front Microbiol* 7, 713, doi:10.3389/fmicb.2016.00713 (2016).
40 Swidsinski, A. *et al.* Active Crohn's disease and ulcerative colitis can be specifically diagnosed and monitored based on the biostructure of the fecal flora. *Inflamm Bowel Dis* 14, 147-161, doi:10.1002/ibd.20330 (2008).
41 Chassard, C. & Bernalier-Donadille, A. H2 and acetate transfers during xylan fermentation between a butyrate-producing xylanolytic species and hydrogenotrophic microorganisms from the human gut. *FEMS Microbiol Lett* 254, 116-122, doi:10.1111/j.1574-6968.2005.00016.x (2006).
42 Bernalier, A. *et al.* Ruminococcus hydrogenotrophicus sp. nov., a new H2/CO2-utilizing acetogenic bacterium isolated from human feces. *Arch Microbiol* 166, 176-183 (1996).
43 Donadille, A. B. Compositions comprising bacterial blautia strains for treating visceral hypersensitivity.
44 Yang, J. *et al.* Xylooligosaccharide supplementation alters gut bacteria in both healthy and prediabetic adults: a pilot study. *Front Physiol* 6, 216, doi:10.3389/fphys.2015.00216 (2015).
45 Tajkarimi, M. & Wexler, H. M. CRISPR-Cas Systems in Bacteroides fragilis, an Important Pathobiont in the Human Gut Microbiome. *Front Microbiol* 8, 2234, doi:10.3389/fmicb.2017.02234 (2017).
46 Lukiw, W. J. Bacteroides fragilis Lipopolysaccharide and Inflammatory Signaling in Alzheimer's Disease. *Front Microbiol* 7, 1544, doi:10.3389/fmicb.2016.01544 (2016).
47 Sanchez, E., Laparra, J. M. & Sanz, Y. Discerning the role of Bacteroides fragilis in celiac disease pathogenesis. *Appl Environ Microbiol* 78, 6507-6515, doi:10.1128/AEM.00563-12 (2012).
48 Wexler, H. M. Bacteroides: the good, the bad, and the nitty-gritty. *Clin Microbiol Rev* 20, 593-621, doi:10.1128/CMR.00008-07 (2007).
49 Ruseler-van Embden, J. G., van der Helm, R. & van Lieshout, L. M. Degradation of intestinal glycoproteins by Bacteroides vulgatus. *FEMS Microbiol Lett* 49, 37-41 (1989).
50 P, O. C. *et al.* The gut bacterium and pathobiont Bacteroides vulgatus activates NF-kappaB in a human gut epithelial cell line in a strain and growth phase dependent manner. *Anaerobe* 47, 209-217, doi:10.1016/j.anaerobe.2017.06.002 (2017).
51 Bamba, T. *et al.*The pathogenic role of Bacteroides vulgatus in patients with ulcerative colitis. *J Gastroenterol* 30 Suppl 8, 45-47 (1995).
52 Matsuda, H. *et al.* Characterization of antibody responses against rectal mucosa-associated bacterial flora in patients with ulcerative colitis. *J Gastroenterol Hepatol* 15, 61-68 (2000).
53 Shiba, T. *et al.* The suppressive effect of bifidobacteria on Bacteroides vulgatus, a putative pathogenic microbe in inflammatory bowel disease. *Microbiol Immunol* 47, 371-378 (2003).
54 Dicksved, J. *et al.* Molecular analysis of the gut microbiota of identical twins with Crohn's disease. *ISME J* 2, 716-727, doi:10.1038/ismej.2008.37 (2008).
55 Lucke, K., Miehlke, S., Jacobs, E. & Schuppler, M. Prevalence of Bacteroides and Prevotella spp. in ulcerative colitis. *J Med Microbiol* 55, 617-624, doi:10.1099/jmm.0.46198-0 (2006).
56 Kinross, J. M. *et al.* The human gut microbiome: implications for future health care. *Curr Gastroenterol Rep* 10, 396-403 (2008).
57 Moore, W. E. & Moore, L. H. Intestinal floras of populations that have a high risk of colon cancer. *Appl Environ Microbiol* 61, 3202-3207 (1995).
58 Leite, A. Z. *et al.* Detection of Increased Plasma Interleukin-6 Levels and Prevalence of Prevotella copri and Bacteroides vulgatus in the Feces of Type 2 Diabetes Patients. *Front Immunol* 8, 1107, doi:10.3389/fimmu.2017.01107 (2017).
59 Rajilic?-Stojanovic?, M. *Diversity of the Human Gastrointestinal Microbiota Novel Perspectives from High Throughput Analyses* PhD thesis, Wageningen University and Research Centre, (2007).
60 Finegold, S. M. *et al.* Pyrosequencing study of fecal microflora of autistic and control children. *Anaerobe* 16, 444-453, doi:10.1016/j.anaerobe.2010.06.008 (2010).
61 Ho, P. L. *et al.* A Novel Selective Medium for Isolation of Bacteroides fragilis from Clinical Specimens. *J Clin Microbiol* 55, 384-390, doi:10.1128/JCM.01988-16 (2017).
62 Sears, C. L., Geis, A. L. & Housseau, F. Bacteroides fragilis subverts mucosal biology: from symbiont to colon carcinogenesis. *J Clin Invest* 124, 4166-4172, doi:10.1172/JCI72334 (2014).
63 Obiso, R. J., Jr., Azghani, A. O. & Wilkins, T. D. The Bacteroides fragilis toxin fragilysin disrupts the paracellular barrier of epithelial cells. *Infect Immun* 65, 1431-1439 (1997).
64 Wells, C. L. *et al.* Bacteroides fragilis enterotoxin modulates epithelial permeability and bacterial internalization by HT-29 enterocytes. *Gastroenterology* 110, 1429-1437 (1996).
65 Riegler, M. *et al.* Bacteroides fragilis toxin 2 damages human colonic mucosa in vitro. *Gut* 44, 504-510 (1999).
66 Akpinar, M. *et al.* Evaluation of the prevalence of enterotoxigenic Bacteroides fragilis and the distribution bft gene subtypes in patients with diarrhea. *Anaerobe* 16, 505-509, doi:10.1016/j.anaerobe.2010.08.002 (2010).
67 Tedjo, D. I. *et al.* The fecal microbiota as a biomarker for disease activity in Crohn's disease. *Sci Rep* 6, 35216, doi:10.1038/srep35216 (2016).
68 Toprak, N. U. *et al.* A possible role of Bacteroides fragilis enterotoxin in the aetiology of colorectal cancer. *Clin Microbiol Infect* 12, 782-786, doi:10.1111/j.1469-0691.2006.01494.x (2006).
69 Boleij, A. *et al.* The Bacteroides fragilis toxin gene is prevalent in the colon mucosa of colorectal cancer patients. *Clin Infect Dis* 60, 208-215, doi:10.1093/cid/ciu787 (2015).
70 Wang, T. *et al.* Structural segregation of gut microbiota between colorectal cancer patients and healthy volunteers. *ISME J* 6, 320-329, doi:10.1038/ismej.2011.109 (2012).
71 Sobhani, I. *et al.* Microbial dysbiosis in colorectal cancer (CRC) patients. *PLoS One* 6, e16393, doi:10.1371/journal.pone.0016393 (2011).

72 de Meij, T. G. *et al.* Characterization of Microbiota in Children with Chronic Functional Constipation. *PLoS One* 11, e0164731, doi:10.1371/journal.pone.0164731 (2016).
73 Hasegawa, S. *et al.* Intestinal Dysbiosis and Lowered Serum Lipopolysaccharide-Binding Protein in Parkinson's Disease. *PLoS One* 10, e0142164, doi:10.1371/journal.pone.0142164 (2015).
74 Minato, T. *et al.* Progression of Parkinson's disease is associated with gut dysbiosis: Two-year follow-up study. *PLoS One* 12, e0187307, doi:10.1371/journal.pone.0187307 (2017).
75 Zhang, M. *et al.* Xylan utilization in human gut commensal bacteria is orchestrated by unique modular organization of polysaccharide-degrading enzymes. *Proc Natl Acad Sci U S A* 111, E3708-3717, doi:10.1073/pnas.1406156111 (2014).
76 Martens, E. C. *et al.* Recognition and degradation of plant cell wall polysaccharides by two human gut symbionts. *PLoS Biol* 9, e1001221, doi:10.1371/journal.pbio.1001221 (2011).
78 Saitoh, S. *et al.* Bacteroides ovatus as the predominant commensal intestinal microbe causing a systemic antibody response in inflammatory bowel disease. *Clin Diagn Lab Immunol* 9, 54-59 (2002).
79 Giongo, A. *et al.* Toward defining the autoimmune microbiome for type 1 diabetes. *ISME J* 5, 82-91, doi:10.1038/ismej.2010.92 (2011).
80 Crost, E. H. *et al.* Utilisation of mucin glycans by the human gut symbiont Ruminococcus gnavus is strain-dependent. *PLoS One* 8, e76341, doi:10.1371/journal.pone.0076341 (2013).
81 Qin, J. *et al.* A human gut microbial gene catalogue established by metagenomic sequencing. *Nature* 464, 59-65, doi:10.1038/nature08821 (2010).
82 Hall, A. B. *et al.* A novel Ruminococcus gnavus clade enriched in inflammatory bowel disease patients. *Genome Med* 9, 103, doi:10.1186/s13073-017-0490-5 (2017).
83 Willing, B. P. *et al.* A pyrosequencing study in twins shows that gastrointestinal microbial profiles vary with inflammatory bowel disease phenotypes. *Gastroenterology* 139, 1844-1854 e1841, doi:10.1053/j.gastro.2010.08.049 (2010).
84 Chua, H. H. *et al.* Intestinal Dysbiosis Featuring Abundance of Ruminococcus gnavus Associates With Allergic Diseases in Infants. *Gastroenterology* 154, 154-167, doi:10.1053/j.gastro.2017.09.006 (2018).
85 Ruchi Singh, T. L. V. during *NKF 2016 Spring Clinical Meeting* Vol. 67 A102 (2016).
86 Joossens, M. *et al.* Dysbiosis of the faecal microbiota in patients with Crohn's disease and their unaffected relatives. *Gut* 60, 631-637, doi:10.1136/gut.2010.223263 (2011).
87 Hoskins, L. C. *et al.* Mucin degradation in human colon ecosystems. Isolation and properties of fecal strains that degrade ABH blood group antigens and oligosaccharides from mucin glycoproteins. *J Clin Invest* 75, 944-953, doi:10.1172/JCI111795 (1985).
88 Martinez-Medina, M. *et al.* Abnormal microbiota composition in the ileocolonic mucosa of Crohn's disease patients as revealed by polymerase chain reaction-denaturing gradient gel electrophoresis. *Inflamm Bowel Dis* 12, 1136-1145, doi:10.1097/01.mib.0000235828.09305.0c (2006).
89 Collins, S. M. A role for the gut microbiota in IBS. *Nat Rev Gastroenterol Hepatol* 11, 497-505, doi:10.1038/nrgastro.2014.40 (2014).
90 Jeffery, I. B. *et al.* An irritable bowel syndrome subtype defined by species-specific alterations in faecal microbiota. *Gut* 61, 997-1006, doi:10.1136/gutjnl-2011-301501 (2012).
91 Rajilic-Stojanovic, M. *et al.* Global and deep molecular analysis of microbiota signatures in fecal samples from patients with irritable bowel syndrome. *Gastroenterology* 141, 1792-1801, doi:10.1053/j.gastro.2011.07.043 (2011).
92 Wang, L. *et al.* Increased abundance of Sutterella spp. and Ruminococcus torques in feces of children with autism spectrum disorder. *Mol Autism* 4, 42, doi:10.1186/2040-2392-4-42 (2013).
93 Steck, N. *et al.* Enterococcus faecalis metalloprotease compromises epithelial barrier and contributes to intestinal inflammation. *Gastroenterology* 141, 959-971, doi:10.1053/j.gastro.2011.05.035 (2011).
94 Zhou, Y. *et al.* Increased Enterococcus faecalis infection is associated with clinically active Crohn disease. *Medicine (Baltimore)* 95, e5019, doi:10.1097/MD.0000000000005019 (2016).
95 Huycke, M. M., Joyce, W. & Wack, M. F. Augmented production of extracellular superoxide by blood isolates of Enterococcus faecalis. *J Infect Dis* 173, 743-746 (1996).
96 Huycke, M. M., Abrams, V. & Moore, D. R. Enterococcus faecalis produces extracellular superoxide and hydrogen peroxide that damages colonic epithelial cell DNA. *Carcinogenesis* 23, 529-536 (2002).
97 Zhou, Y. *et al.* Association of oncogenic bacteria with colorectal cancer in South China. *Oncotarget* 7, 80794-80802, doi:10.18632/oncotarget.13094 (2016).
98 Swidsinski, A. *et al.* Mucosal invasion by fusobacteria is a common feature of acute appendicitis in Germany, Russia, and China. *Saudi J Gastroenterol* 18, 55-58, doi:10.4103/1319-3767.91734 (2012).
99 Tahara, T. *et al.* Fusobacterium detected in colonic biopsy and clinicopathological features of ulcerative colitis in Japan. *Dig Dis Sci* 60, 205-210, doi:10.1007/s10620-014-3316-y (2015).
100Strauss, J. *et al.* Invasive potential of gut mucosa-derived Fusobacterium nucleatum positively correlates with IBD status of the host. *Inflamm Bowel Dis* 17, 1971-1978, doi:10.1002/ibd.21606 (2011).
101 Tjalsma, H. *et al.* A bacterial driver-passenger model for colorectal cancer: beyond the usual suspects. *Nat Rev Microbiol* 10, 575-582, doi:10.1038/nrmicro2819 (2012).
102 Keku, T. O. *et al.* Fusobacterium spp. and colorectal cancer: cause or consequence? *Trends Microbiol* 21, 506-508, doi:10.1016/j.tim.2013.08.004 (2013).
103 Allen-Vercoe, E. & Jobin, C. Fusobacterium and Enterobacteriaceae: important players for CRC? *Immunol Lett* 162, 54-61, doi:10.1016/j.imlet.2014.05.014 (2014).
104 McCoy, A. N. *et al.* Fusobacterium is associated with colorectal adenomas. *PLoS One* 8, e53653, doi:10.1371/journal.pone.0053653 (2013).
105 Han, Y. W. Fusobacterium nucleatum: a commensal-turned pathogen. *Curr Opin Microbiol* 23, 141-147, doi:10.1016/j.mib.2014.11.013 (2015).
106 Castellarin, M. *et al.* Fusobacterium nucleatum infection is prevalent in human colorectal carcinoma. *Genome Res* 22, 299-306, doi:10.1101/gr.126516.111 (2012).
107 Marchesi, J. R. *et al.* Towards the human colorectal cancer microbiome. *PLoS One* 6, e20447, doi:10.1371/journal.pone.0020447 (2011).
108 Kostic, A. D. *et al.* Genomic analysis identifies association of Fusobacterium with colorectal carcinoma. *Genome Res* 22, 292-298, doi:10.1101/gr.126573.111 (2012).
109 Kostic, A. D. *et al.* Fusobacterium nucleatum potentiates intestinal tumorigenesis and modulates the tumor-immune microenvironment. *Cell Host Microbe* 14, 207-215, doi:10.1016/j.chom.2013.07.007 (2013).
110 Rubinstein, M. R. *et al.* Fusobacterium nucleatum promotes colorectal carcinogenesis by modulating E-cadherin/beta-catenin signaling via its FadA adhesin. *Cell Host Microbe* 14, 195-206, doi:10.1016/j.chom.2013.07.012 (2013).
111 Flanagan, L. *et al.* Fusobacterium nucleatum associates with stages of colorectal neoplasia development, colorectal cancer and disease outcome. *Eur J Clin Microbiol Infect Dis* 33, 1381-1390, doi:10.1007/s10096-014-2081-3 (2014).
112 Taras, D. *et al.* Reclassification of Eubacterium formicigenerans Holdeman and Moore 1974 as Dorea formicigenerans gen. nov., comb. nov., and description of Dorea longicatena sp. nov., isolated from human faeces. *Int J Syst Evol Microbiol* 52, 423-428, doi:10.1099/00207713-52-2-423 (2002).
113 Saulnier, D. M. *et al.* Gastrointestinal microbiome signatures of pediatric patients with irritable bowel syndrome. *Gastroenterology* 141, 1782-1791, doi:10.1053/j.gastro.2011.06.072 (2011).
114 Schirmer, M. *et al.* Linking the Human Gut Microbiome to Inflammatory Cytokine Production Capacity. *Cell* 167, 1897, doi:10.1016/j.cell.2016.11.046 (2016).
115 Nomura, T. *et al.* Mucosa-associated bacteria in ulcerative colitis before and after antibiotic combination therapy. *Aliment Pharmacol Ther* 21, 1017-1027, doi:10.1111/j.1365-2036.2005.02428.x (2005).
116 Megraud, F. *et al.* Haemophilus species in the human gastrointestinal tract. *Eur J Clin Microbiol Infect Dis* 7, 437-438 (1988).
117 Kasai, C. *et al.* Comparison of human gut microbiota in control subjects and patients with colorectal carcinoma in adenoma: Terminal restriction fragment length polymorphism and next-generation sequencing analyses. *Oncol Rep* 35, 325-333, doi:10.3892/or.2015.4398 (2016).
118 Ley, R. E. Gut microbiota in 2015: Prevotella in the gut: choose carefully. *Nat Rev Gastroenterol Hepatol* 13, 69-70, doi:10.1038/nrgastro.2016.4 (2016).
119 De Filippis, F. *et al.* Unusual sub-genus associations of faecal Prevotella and Bacteroides with specific dietary patterns. *Microbiome* 4, 57, doi:10.1186/s40168-016-0202-1 (2016).
120 Wu, G. D. *et al.* Linking long-term dietary patterns with gut microbial enterotypes. *Science* 334, 105-108, doi:10.1126/science.1208344 (2011).
121 Larsen, J. M. The immune response to Prevotella bacteria in chronic inflammatory disease. *Immunology* 151, 363-374, doi:10.1111/imm.12760 (2017).
122 Fugmann, M. *et al.* The stool microbiota of insulin resistant women with recent gestational diabetes, a high risk group for type 2 diabetes. *Sci Rep* 5, 13212, doi:10.1038/srep13212 (2015).
123 Pedersen, H. K. *et al.* Human gut microbes impact host serum metabolome and insulin sensitivity. *Nature* 535, 376-381, doi:10.1038/nature18646 (2016).
124 Scher, J. U. *et al.* Expansion of intestinal Prevotella copri correlates with enhanced susceptibility to arthritis. *Elife* 2, e01202, doi:10.7554/eLife.01202 (2013).
125 Bag, S. *et al.* Complete Genome Sequence of Collinsella aerofaciens Isolated from the Gut of a Healthy Indian Subject. *Genome Announc* 5, doi:10.1128/genomeA.01361-17 (2017).
126 Salonen, A. *et al.* Gastrointestinal microbiota in irritable bowel syndrome: present state and perspectives. *Microbiology* 156, 3205-3215, doi:10.1099/mic.0.043257-0 (2010).
127 Lambeth, S. M. *et al.* Composition, Diversity and Abundance of Gut Microbiome in Prediabetes and Type 2 Diabetes. *J Diabetes Obes* 2, 1-7, doi:10.15436/2376-0949.15.031 (2015).
128 Zhang, X. *et al.* Human gut microbiota changes reveal the progression of glucose intolerance. *PLoS One* 8, e71108, doi:10.1371/journal.pone.0071108 (2013).
129 Lahti, L. *et al.* Associations between the human intestinal microbiota, Lactobacillus rhamnosus GG and serum lipids indicated by integrated analysis of high-throughput profiling data. *PeerJ* 1, e32, doi:10.7717/peerj.32 (2013).
130 Karlsson, F. H. *et al.* Symptomatic atherosclerosis is associated with an altered gut metagenome. *Nat Commun* 3, 1245, doi:10.1038/ncomms2266 (2012).
131 Feng, Q. *et al.* Gut microbiome development along the colorectal adenoma-carcinoma sequence. *Nat Commun* 6, 6528, doi:10.1038/ncomms7528 (2015).
132 Yan, Q. *et al.* Alterations of the Gut Microbiome in Hypertension. *Front Cell Infect Microbiol* 7, 381, doi:10.3389/fcimb.2017.00381 (2017).
133 David, L. A. *et al.* Diet rapidly and reproducibly alters the human gut microbiome. *Nature* 505, 559-563, doi:10.1038/nature12820 (2014).
134 Rautio, M. *et al.* Reclassification of Bacteroides putredinis (Weinberg et al., 1937) in a new genus Alistipes gen. nov., as Alistipes putredinis comb. nov., and description of Alistipes finegoldii sp. nov., from human sources. *Syst Appl Microbiol* 26, 182-188, doi:10.1078/072320203322346029 (2003).
135 Rautio, M. *et al.* Bacteriology of histopathologically defined appendicitis in children. *Pediatr Infect Dis J* 19, 1078-1083 (2000).
136 Louis, S. *et al.* Characterization of the Gut Microbial Community of Obese Patients Following a Weight-Loss Intervention Using Whole Metagenome Shotgun Sequencing. *PLoS One* 11, e0149564, doi:10.1371/journal.pone.0149564 (2016).
137 Qin, J. *et al.* A metagenome-wide association study of gut microbiota in type 2 diabetes. *Nature* 490, 55-60, doi:10.1038/nature11450 (2012).
138 Jiang, H. *et al.* Altered fecal microbiota composition in patients with major depressive disorder. *Brain Behav Immun* 48, 186-194, doi:10.1016/j.bbi.2015.03.016 (2015).
139 Van de Merwe, J. P. *et al.* The obligate anaerobic faecal flora of patients with Crohn's disease and their first-degree relatives. *Scand J Gastroenterol* 23, 1125-1131 (1988).
140 Van de Merwe, J. P. & Stegeman, J. H. Binding of Coprococcus comes to the Fc portion of IgG. A possible role in the pathogenesis of Crohn's disease? *Eur J Immunol* 15, 860-863, doi:10.1002/eji.1830150823 (1985).

Examples of our Genetic Profiles:

FEMgen: Sporadic breast cancer

OSTEOgen: Osteoporosis

THROMBOgen: Thrombosis

PROSTATEgen: Prostate cancer

DETOXgen: Detoxification capacities

OXIgen: Oxidative stress

DENTYgen: Periodontitis

NEUROgen: Neurodegenerative diseases

CARDIOgen: Cardiovascular diseases

MACULAgen: Age-Related Macular Degeneration

LIPIDgen: Lipid metabolism disorders

DIABETOgen: Diabetes type II

COLOgen: Sporadic colon carcinoma

ALOPECIAgen: Androgenetic alopecia

EMOgen: Emotional instability

SKINgen: Skin health

WEIGHTgen: Weight control

WELL-BEING: Anti-aging

NICOTINEgen: Nicotine addiction

38, rue Hiehl · Z.A.C. Laangwiss · L-6131 Junglinster
Tel: +352 780 290-1 · Fax +352 788 894 · contact@labo.lu
www.labo.lu

LABORATOIRES RÉUNIS