IJMSNHEM - MicroBiome

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Evidence Based Literature to Protect and Explore Natural Medicine since 1996

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The MicroBiome 2020
Brain Hormones Made in the GUT:
- Serotonin - Your Happy Hormone
- GABA - Controls Stress + Anxiety
- Dopamine - For Motivation, Pleasure
- Oxytocin - for Bonding + Control of Self
- CCK, PYY, GLP-1, GIP + 5-HT
and many more ESSENTIAL
Hormones are Made in the GUT

The Drug Companies Have Sought to Use
\textit{SIN}-thetic Completely UnNatural Patent
Medicines to Alter the Brain Hormones By
- Blocking, Substituting, Inhibiting, Augmenting,
- Suppress, Repress, Obstruct, Interfere, and Impede Brain Hormones and Function
Rather Than Balance the Gut
They Sought to Profit From the Mentally ILL
\textit{The Side Effects Alone make Vast Profit}

All Diseases Begin in the GUT
Mental Health Begins in the Gut

We Germs Make Healthy Hormones

Only By Stabilizing the Gut Flora Can We Start To Treat Mental Health + All Disease
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There are over a Billion Trillion Genes in One Person’s MicroBiome Making this a Vastly Complicated Fractal Environment That can Only be Treated with Natural Means
**There are Over 100 TRILLION GERMS Essential for Health in and on your Body.**

Germs *do not really cause disease as much as Un-Managed GERMS cause disease.*

By Professor of Medicine Desire’ Dubounet

Our bodies are not just human flesh. We are a galaxy of micro-organisms, that’s right germs that are essential, Yes, **Essential** for life. Without these germs we die. We live in a mutually dependent symbiotic relationship with trillions of germs that we call our microbiome.

There are more than ten times more critically needed germ cells in one human than human cells. More than 60% of our energy field in made by these germs. Over 10% of our body weight is made of these germs.

These germs make the crucial hormones, neurotransmitters, vitamins and more nutrients necessary for life. These germs regulate and balance the health of our body, mind and spirit. These germs are us. These germs are a vital indispensable part of our bodies. Working together, we are a team striving for balance health and wellness.
We must rethink the word germ. We were wrongfully taught to fear all germs when it is a weak immune system that we need fear. When we weaken our immune system the germ balance can be upset and bad germs can flourish.

There are bad germs that feed on **SIN**thetic Sweeteners and Chemicals. There are bad germs that feed on processed sugar and processed foods. These bacteria and fungi can take over your brain and make you CRAVE the foods that feed them. Yes this is true. These bad germs can CONTROL YOU. They can make you into a mindless puppet craving the foods that further enslave you. And these bad germs shorten your attention span, lower your IQ and memory, and make you ill in a hundred ways.

I know this sounds like a Hollywood Horror movie, but this is scientific fact. Some people are so addicted and enslaved, they cannot hear this message. Anything that threatens their bad germ masters, the bad germs will stop you from hearing, and stop you from getting healthy and free. If you have ever watched Jimmy Kimmel on late night TV’s skit on taking away Halloween candy from children, you have witnessed extreme over reaction of a body who is heavily addicted. You would think that such reaction is only reserved for Meth Heads, but you would be wrong. The craving and dependency of the person with the bad bowel flora is quite pronounced.

E-coli bacteria are found in everyone’s gut and on everyone’s skin. They are needed for immune regulation and nutrient manufacturing especially GABA. But if you get over exposed to a virulent form of E-Coli and your immune
system is weak the E-coli can become opportunistic and start to grow past safe levels.

All of life is about BALANCE. Moderation in all things. You can get sick from excess germ exposure, and you can get sick from too little germ contact. Germ-phobia and over reaction is not the answer.

The gut bacteria is in a constant state of flux. The bowel flora changes every 15 minutes. Just one atom of Xeon can prompt major gut flora change. It is very sensitive. So it becomes a battle and requires attention to diet and lifestyle.

**Need to Know Facts:**

1. Our life and health depends on a Symbiotic Germ Balance in our bodies
2. We must have at least 25% of our diet in Plant fiber not found in meat
3. We must Avoid **SIN**thetic foods and chemicals,
4. We must Avoid Processed Sugars and Processed Foods
5. Avoid any food boiled in oil.
6. We should NOT be overly Afraid of Germs.
7. We need to take care of our Immune System

Hippocrates was right: Let food be thy medicine

The Mind - Gut Bond is the Basis of Life
To correct your Bowel Flora and Start Good Mental Health

1. Avoid *SIN*thetic foods, chemicals and drugs especially antibiotics, avoid foods boiled in Oil, Avoid all fiber free processed sugars, Avoid all Chemical sweeteners, Avoid Meat where they used Antibiotics + other Farm *SIN*thetic Chemicals
2. Substitute Fine Apple Sauce for Sugar in ALL Recipes
3. Destroy excess bad bacteria with the Get Well Remedy 3 pills twice a day, or other strong 3 day intestinal cleanse with Activated Charcoal, Honey and Pau Dárco Tea
4. Eat prebiotics for 3 days after intestinal cleanse
5. Chew Foods and always eat smaller meals slowly
6. Exercise and Yoga
7. Manage stress and use the Correct Hemispheric breathing techniques to help balance the Brain
8. Eat Probiotics at every meal and Probiotic Yogurt before bed
9. Take the MicoBiome Reboot 3 pills twice a day for 3 days
10. Natural B 15 -- 3 pills at bed
11. Eat some fermented foods like Kim Chi everyday
12. Eat 25 grams of fiber every day from fruits and vegetables
13. Drink 8 glasses of water a day
14. Avoid excess alcohol or stimulants
15. Use natural antibiotics and antifungals instead of *SIN*thetic ones
16. Do a probiotic enema once a month, With coffee if fatigued – add MicoBiome Reboot to the enema if you can.
17. Find a natural medicine doctor for networking and to help lessen your medication as you improve. As you lessen your medication you often have withdrawal symptoms from the drug addiction and or dependency. Deal with this with counselling, networking and positive family.
Step 1 Learn what not to eat

**SUPER IMMUNE Diet Tips**

STARTS With

**What NOT To EAT**

1. AVOID Synthetic Foods
2. AVOID Hi Glycemic Foods
3. AVOID Processed Foods
4. AVOID White Sugars
5. AVOID Foods Boiled in Oil
6. AVOID Nitrite/Nitrate meat

---

**THE FIVE UNHEALTHY WHITES**

Avoid excess use
Use sparingly not Daily

- WHITE RICE
- WHITE FLOUR
- WHITE SUGAR
- White Pork
- White Potato
**IJMSNHEM - MicroBiome**

**Step 2 – Kill the Bad Bowel Bacteria**

3 days to Kill Off Bad Bacteria + Prepare to Restore a Balanced Bowel Flora

3 pills in Morning- 3 at night

**Only Nature Knows**

Supported by IMUNE

www.IMUNE.net

Get Well

**Herbal Supplement**

3 Pills at NOON

3 pills in Morning- 3 at night

Once a Day

Onion and Garlic soup

Lots of Water and Herb Teas,
Fast as best you can
Use Soups, Eat Apples
Use these 3 days to relax the bowel and Cleanse the Bad Bacteria and Fungus

**Prebiotic Foods**

**Foods High in Prebiotics**

- Apples
- Jerusalem artichokes
- Onions
- Leeks (the bulb)
- Jicama
- Sweet potatoes

Take the Charcoal Separately for it to absorb the toxic die off of the bad Bacteria and fungus
Get Well Formula is a source of strong NATURAL antimicrobial compounds which can contribute to the healthy functioning of the gastrointestinal GI system. Get Well is a source of NATURAL berberine and NATURAL hydrastine these natural antimicrobial compounds kill bad bacteria more effectively while do only little harm to good bacteria in the human microbiome.

Get Well

Antimicrobial formula
Anti-inflammatory
For a Healthy Microbiome
Kills bad bacteria

☑️ Common Allergen FREE
☑️ UV protective packaging
☑️ Synthetic FREE

by Professor Desire’ Dubbonet

Natural berberine from Mahonia aquifolium
Natural hydrastine from Hydrastis canadensis
Garlic for the better absorption of the ingredients

QUANTUM BIOFEEDBACK ENERGETIC SUPERCHARGED

OnlyNatureKnows.com  info@onlynatureknows.com

Official webshop

IMUNE
INTERNATIONAL MEDICAL UNIVERSITY
OF NATURAL EDUCATION
Step 3 – Reboot the Good Bowel Flora

Use the MicroBiome Reboot formula for 3 Days
3 pills at Noon, 3 Pills at Bed and use these foods
ProBiotic Foods that You Work into your Daily Diet

Important: Take the MicroBiome Reboot 1 hour after a meal with 12 oz of water. This will help the new Bacteria get past the Stomach Acid Barrier.
Newest research have shown dopamine and all neurotransmitters created by the gut microbiome they are in close connection and they influence overall health and how the brain expresses it’s activities. Microbiome Reboot helps you to reboot to a healthier microbiome with NATURAL herbs and NATURAL healthy bacteria for the intestines.

**Microbiome Reboot**

Promotes good bacteria  
For a Healthy Microbiome  
Kills bad bacteria

- Common Allergen FREE  
- UV protective packaging  
- Synthetic FREE

Contains NATURAL herbs and NATURAL healthy bacteria which promotes a healthy bowel flora and supports overall immunity.

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IMUNE  
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Basic Nutrition

**WHAT TO EAT**

1. Eat Natural Foods with little preservatives
2. Eat more fruits, seed products, leafy greens, salads
3. Let Fruit be your Sweetener,
4. Drink ONLY 100% Fruit juice diluted with water
5. Boil foods in WATER, NOT OIL
6. Use fresh, cold processed UNHEATED olive oil, sunflower oil, safflower oil etc.
7. Less Cooking, Use stir fry well washed veggies
8. Foods made with Love and Nature is Blessed
    Nutrition, Foods made and eaten with Hate and Anger are poisons.
9. Celebrate each meal with friends, family or at least your joyous self. Celebrate
10. Listen to your inner self what to eat, and when to stop, do not eat with your eyes

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**THE SIX UNHEALTHY WHITES**

**If You Have Cancer Do NOT EAT These Foods**

- White Sugar
- White Flour
- White Pork
- White Potato
- Milk
- White Rice
10x HAPPY Increase Serotonin

Green Smoothie energy boost, zap!
Epsom salt calming
Smiling releases happy hormones

Walnuts – Omega 3 brain nutrients
Almonds – Magnesium brain food
Spend time in nature

Leaf Greens boost energy
Water Hydration more energy less stress
Walking – clears mind boosts serotonin

6 Great Foods That Increase Dopamine Levels
Newest research have shown serotonin and microbiome close connection and influencing each other. Seroto Liquitrophic made with Desire’s old Seroto recipe and natural serotonin. Destroys the harmful fungal form of candida in the intestines.

Seroto Liquitrophic

Promotes positive mood
Antifungal activity
For a Healthy Microbiome
Dopamine support

Griffonia simplicifolia is an excellent source of NATURAL serotonin. The formula contains NATURAL dopamine as well.

Step 5 Learn and Obey the Rules of Digestion and Practice the Rules of the Stomach
Avoid SInthetics, Fatty,
Processed, Boiled Oil, +
Hi-Glycemic Foods
Eat High Nutrient Fiber Fruits,
Seeds, Legumes + Veg, little meat
Chew Chew
Mix Salvia with Food

FOSSIL LAP DIGESTION RULES

Autonomic Nerves - Reduce Stress
+ Learn to Diaphragm Breath
Learn Vagus Nerve Massage
Fruits, Fluids, Melons Alone- Relax During
+ After Meals, Eat Small Meals Slowly
Celebrate Life with a Meal

Do Not Smoke-Limit Alcohol
Eat low-fat, grains, fruits + veg
Avoid all Processed foods
like Sugars + Meats
Eat Low Fat high Fiber,
Exercise + Lots of Water
Learn Valve of Huston
Massage
Get both insoluble and
soluble fiber, Use good
Probiotics Avoid any Antibiotics
or meat with Antibiotics
Use Natural Medicines whenever possible
SINthetic Patents as a Last Resort

1. Drink Water. It's what you're made of!
2. Do your exercise!
3. Breathe fresh air.
4. Go outside when the sun is out.
5. Learn to relax.
6. Eat your fruits.
7. Eat your vegetables.
8. Eat Whole Grains.
9. White if you choose meat.
10. Get to bed on time.
RULES OF THE STOMACH

1. Fluids alone (no more than 4 oz. fluid with a meal, or 2 hours after a meal)
2. No coffee at meals (wait for 1.5 to 2 hours after or 1 hour before eating)
3. No milk with meals (wait for 1.5 to 2 hours after or 1 hour before eating)
4. Fruits alone (wait for 1.5 to 2 hours after or 1 hour before eating)
5. Melons alone (wait for 1.5 to 2 hours after or 1 hour before eating)
6. Small meal is better. Quality of nutrition, not quantity
7. Slow meals. Savor, enjoy, rejoice, and celebrate the meal
8. Eat for nutrition, not for stimulation. Eat when hungry, not when bored.
9. Rest comfortably after eating for at least 35 to 45 min to maximize stomach function
10. Make and eat food with love and kindness, no violent or negative emotions
11. No antacids
12. Do not sleep for 3 hours after eating.

ALWAYS CHEW YOUR FOOD
Video References:

How do you know your microbiome is bad and how to fix it
How to fix your Bowel Flora

Bigotry Started with Ancient Microbiome Fear

Big Pharma Destroys Your MicroBiome and produces mental disease
Big Sugar Destroys your MicroBiome and produces mental disease
Plant Fiber is needed by the body for health
Bad Evil Gut Flora Take Over the Brain and make money for the EVIL Ultra Rich
Microbiome bad gut flora takes over the Brain and makes disease
Mental Health and the Microbiome intro
Four Simple Mental Health Prep Exercises
Bad Gut Bacteria make Obese Patients by taking over the brain

Bad Bacteria Take over the Brain

Evil Aliens plant sugar, corn, potato with bacteria that makes cravings, for us to be food

The Microbiome Diet:

http://medicalexposedownloads.com/PDF/Great%20Foods%20that%20Increase%20Dopamine%20Levels%20for%20depression%20and%20lack%20of%20motivation.pdf


Recipes and Tips for a Healthy Gut Flora to Stop Disease
Abstract

Contemporary science writing suffers from errors in quotations and misattributions. Given the importance of the microbiome to virtually every branch of science and medicine, its early origins and historical references are vital. Regardless of technological applications – culture technique or next-generation metagenomics – accurate referencing is essential to the scientific pursuit of truth. Despite claims and inferences to the contrary, the rich history of the study of microbiota and the microbiome didn’t begin in 2001; many lessons can be learned by closely examining the history of the gut-brain-microbiota connection, including the undervalued role of early pioneers in this field.

Keywords

Microbiome
Allergy
Dubos
Mental
Brain
Depression

“Let food be thy medicine and medicine be thy food”

Who among us hasn’t read the famous quote concerning the medicinal aspects of food within science writing and on the big screen at conferences? The oft-cited quote above is continuously attributed to Hippocrates within peer-reviewed writing. However, there isn’t a shred of evidence that Hippocrates conveyed this message verbally or in writing. Moreover, all of the available evidence indicates that such a quote – conflating diet and medicines – was developed more recently, and in any case, would be completely at odds with Hippocratic thinking [1]. Since
Hippocrates is revered in western culture, the quote is often oriented to a slant such that it is possible to forgo “medicines”.
The factual origins of terms and phrases are important for a variety of reasons, including the ways in which they can be insinuated into culturally-determined science writing. Stating that an individual coined a term isn’t a vague claim – it should stand up to scrutiny no less than the data presented in the Results Section of an original article. The science writer is informing the reader of facts; in the case of ‘coining’, the writer should be 100 percent sure that, indeed, person X was the first to use and/or formulate a word or phrase. Coining is completely distinct from defining or popularizing a term.

Such is the case within the microbiome zeitgeist. For example, it is continuously claimed that the term microbiome was ‘coined’ by Nobel laureate-microbiologist Joshua Lederberg in a 2001. This statement of coinage is presented as fact in 100 s of recent research papers, including those in journals devoted to pediatrics [2], allergy/immunology [3] and even in papers originating from the United States National Institutes of Health, Human Microbiome Project [4], [5]. In an article purporting to set the record straight on microbiome terminology, it is even claimed that the term microbiota was defined for the first time by Lederberg in 2001 [6]. Remarkably, a ‘History of Medicine’ article in a recent Annals of Internal Medicine issue makes this same claim that Lederberg coined the term in 2001 [7]. Despite these claims, the evidence is crystal clear – Lederberg did not coin the term microbiome, nor did he define or coin the term microbiota. Indeed, microbiota is a basic microbiology term in common use for at least 50 years. For example, when germ-free and specific pathogen free animal models were incorporated into common laboratory practices in the 1960s, it was with the specific aim to determine the “selected microbiota compatible with sustained health” [8]; Lederberg didn’t need to define microbiota, the word never even appeared once in his oft-cited 2001 article [9]. Prior to 2001, the term microbiome was also in use, mostly to infer a very small ecological niche incorporating plant and animal life. Using the search engine Google Books and holding the search to pre-2001 entries will reveal the flavor of usage. Most notably, one particular discussion of the microbiome – in 1988 – provided a specific definition that is directly in line with its current usage in microbiology: “A convenient ecological framework in which to examine biocontrol systems is that of the microbiome. This may be defined as a characteristic microbial
community occupying a reasonably well defined habitat which has distinct physico-chemical properties. The term thus not only refers to the microorganisms involved but also encompasses their theatre of activity.” [10]

This history was brought to light by Alan C. Logan (who has written extensively on the history of microbiota and mental health [11], [12], [13]) and is discussed in further detail at the blog of noted microbiome expert, University of California Professor Jonathan A. Eisen [14]. Collections such as Google Books and Google Scholar allow for relatively simple ways to determine some of the early origins of terms and who said what, when. This is not a matter of semantics and cannot be confused with administrative referencing/citation errors that inevitably find their way through manuscript proofing stages; misquotes and misattributions are a plague in modern science writing, with 15–20% of articles containing major quotation errors [15], [16].

It matters because, as described in reference to the Hippocrates non-quote above, the consequences can lead to ‘scientific myth’ [17]. At the extreme end this could influence policy and practice [1]. However, even at its most fundamental level, factual science referencing is a matter of ethics. Providing credit where credit is due. When an erroneous attribution is afforded to one researcher, especially a term or quotation in common parlance, the individual or group of individuals – the legitimate source – will remain in the scientific shadows [18].

The oversight of scientists Linda R. Hegstrand and colleague Roberta Jean Hine in the annals of the gut-brain axis, mental health and allergy, provides a clear example of why referencing matters. In 1986, the pair published a groundbreaking study wherein they demonstrated significant differences in hypothalamic histamine levels between germ-free and conventionally raised animals. Put simply, they proved that microbes influence brain chemistry [19]. Enormous implications; total citations to date = 3. The gut-brain-microbiota axis is a rich topic of conversation at the moment. Claims that the term ‘microbiome’ was coined in 2001 lead to inferences surrounding ‘discovery’ and by extension, obscure the wellspring of ideas and original findings. It’s past time to fix this.

The contemporary reader might be unwittingly led to believe that a rich history in the study of microbiota didn’t exist prior to 2001. Of course the cost reduction of high throughput sequencing technology and the application of proteomics, metabolomics, and epigenomics has propelled the microbiome revolution into a truly exciting era for pediatric allergy and
immunology. These advances provide hope for prevention, and precise, personalized medical treatments. However, lack of factual referencing can obscure important and highly-relevant findings from the past. Young scientists may be unaware that Rene Dubos studied germ-free and specific-pathogen-free mice for over a decade, determining the interactions between microbiota and factors such as nutrition, stress, maternal care, housing conditions, social interactions and sanitation, on immune function and health over the life course [20].

As pointed out by psychiatrist Iago Galdston: “The essential deficiencies in academic medical history derive from its commitment to the “great man, great discoveries view of medical history”. [21]. The erroneous claim that a Nobel laureate coined the term microbiome feeds into this historical commitment. Is there no legacy for the thoughtful definition of the microbiome by those less well-acclaimed? Hippocrates gets credited for saying things he didn’t say, while Hegstrand and Hine remain unreferenced. Science is itself a compass oriented toward seeking truth. This direction-finding needle is compromised when scientific articles include rinse-and-repeat claims concerning coining of terms and the fountainheads of discovery. The Introduction/Background sections of all articles – reviews and original work – include choices of referencing. Those choices are a matter of ethics. And truth.

Conflict of interest

SLP reports the following: Scientific Advisory Board and speakers fees from Danone Nutricia, Schiphol, Netherlands and Nestlé Nutrition Institute, Lausanne, Switzerland; compensated consultant to Bayer Pharmaceuticals, Whippany, NJ, USA.

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The Population of Microorganisms in your Gut Predicts your Personality.

Abstract: The gut microbiome has a measurable impact on the brain, influencing stress, anxiety, depressive symptoms and social behavior. This microbiome-gut-brain axis may be mediated by various mechanisms including neural, immune and endocrine signaling. To date, the majority of research has been conducted in animal models, while the limited number of human studies has focused on psychiatric conditions. Here the composition and diversity of the gut microbiome is investigated with respect to human personality. Using regression models to control for possible confounding factors, the abundances of specific bacterial genera are shown to be significantly predicted by personality traits. Diversity analyses of the gut microbiome reveal that people with larger social networks tend to have a more diverse microbiome, suggesting that social interactions may shape the microbial community of the human gut. In contrast, anxiety and stress are linked to reduced diversity and...
an altered microbiome composition. Together, these results add a new dimension to our understanding of personality and reveal that the microbiome-gut-brain axis may also be relevant to behavioral variation in the general population as well as to cases of psychiatric disorders.

There may be no actual butterflies in your stomach, but there are approximately 100 trillion microorganisms in your gut. Collectively, these microorganisms — a mixture of bacteria, viruses, fungi, and protozoa — are known as the microbiome. It’s increasingly clear that the microbiome influences mental and physical health. Now, scientists have taken this topic a step further and linked the microbiome to the likelihood of specific personalities.

Personality is both inherited and influenced by one’s environment. And the environment inside humans may matter just as much as the external environment, argues Katerina Johnson, a research associate at the University of Oxford.

Her research, which will be published in the March edition of the Human Microbiome Journal, suggests that gut microbiome composition may be related to differences in personality — and that the diversity of the microbes in your gut could help predict these traits.

The study reveals that how social you are may be linked to the diversity of your microbiome, with higher diversity indicating more pro-social personalities. The opposite — a low level of diversity — may be indicative of neuroticism.

The findings add a new dimension to the science of personality — and suggest that a better understanding of microbiome-gut-axis could lead to new therapies for conditions that affect mental health, Johnson says. Social interactions, where we spend our time, and what we eat all affect the gut microbiome, and likely are “affecting our behavior and psychological well-being in currently unknown ways,” she says.

THE GUT-PERSONALITY LINK

The results add to a growing body of research which links different gut bacteria with autism, which can affect social abilities, while other recent research suggests that people with depression also have different gut bacteria than those without. The link between social stress and gut bacteria was also explored in a fascinating 2019 study, in which scientists gave rats a transplant
of gut bacteria from rats that show depressive behavior. The previously not-depressed rats began to show stressed-out behavior after the transplant.

This new study doesn't focus on a particular brain condition. Instead, it looks at the link between the composition of the human microbiome and broad personality traits.

A sample of 655 adults were given at-home “gut kits” made by a company called uBiome (the company is now bankrupt). Before the startup was raided by the FBI, it made its name analyzing the DNA of the microorganisms found in poop. Fecal samples of this kind are considered sufficiently representative of the composition of the gut microbiome.

People with larger social networks tend to have a more diverse microbiome.

The study participants also filled out an online questionnaire that surveyed their behavioral traits, sociodemographic factors, diet, health, and lifestyle choices. Their personality traits were assessed with a standard “Big Five” personality assessment. The researcher also assessed participants' general tendency to feel anxious, as well as the Autism Spectrum Quotient, to measure the degree to which an individual displayed autistic-like behavior.

The results reveal that people with larger social networks tend to have a more diverse microbiome, while lower diversity was associated with increased levels of stress and anxiety. People who reported that they typically don’t sleep well also had a less diverse microbiome.

Interestingly, the results also show that people who eat food with more naturally occurring probiotics, like yogurt and sauerkraut, had significantly lower levels of anxiety, stress, and neuroticism. They were also less likely to suffer from a mental illness.

The same did not hold true for people who consumed probiotics in supplement form instead.

Adventurous eaters, on average, had greater gut diversity, as well — further supporting the idea that microbiome health can be improved by diet.

**WHAT DRIVES THE LINK?**

Certain bacteria species were more abundant in individuals who were more social: Those that belong to the
genera Akkermansia, Lactococcus, and Oscillospira. Johnson notes that previous research found that children with autism also have a reduction of Lactococcus and Oscillospira — that suggests the bacteria may be linked to social difficulties in autism.

Two other bacteria genera, Desulfovibrio and Sutterella, meanwhile, were less abundant in less sociable people.

Taken together, the results indicate that some bacterial genera may be more strongly linked to behavior than others. Future investigation of their effects on social behavior in animal models could lead to potential new therapies for autism, Johnson says. While it offers clues to the gut-brain axis, the study does not answer whether microbiome diversity drives personality traits, or vice versa. In fact, the research suggests that it may be a two-way street, with behavior shaping the composition of the gut microbiome, and certain gut microbes affecting the body’s stress response.

There are a number of possible reasons why there’s an interaction between the gut microbial community and the brain. Scientists think what’s in the gut could be communicating to the brain through neural, immune, and endocrine pathways — but they don't have the data to prove it. What we do know is that gut microorganisms can produce various neuroactive chemicals, and that certain psychiatric conditions often come hand-in-hand with gastrointestinal problems. More human studies are needed to know for sure — until recently, most research has involved animal models. But it does appear that our life on the outside affects life on the inside, and vice versa. How we can leverage that
knowledge to live better remains to be seen, but at least we will get to know our guts in the process.

The microbiome as a human organ

Abstract

The human organism is a complex structure composed of cells belonging to all three domains of life on Earth, Eukarya, Bacteria and Archaea, as well as their viruses. Bacterial cells of more than a thousand taxonomic units are condensed in a particular functional collective domain, the intestinal microbiome. The microbiome constitutes the last human organ under active research. Like other organs, and despite its intrinsic complexity, the microbiome is readily inherited, in a process probably involving ‘small world’ power law dynamics of construction in newborns. Like any other organ, the microbiome has physiology and pathology, and the individual (and collective?) health might be damaged when its collective population structure is altered. The diagnostic of microbiomic diseases involves metagenomic studies. The therapeutics of microbiome-induced pathology include microbiota transplantation, a technique increasingly available. Perhaps a new medical specialty, microbiomology, is being born.

Keywords:

Human organ
microbiome
microbiomology
transplantation

We are pleased to introduce the present collection of short reports which correspond to the presentations of the 18th Scientific Symposium of the Lilly Foundation Spain, entitled ‘Microbiome: Deciphering the Last Organ of the Human Body’. This title emphasized an important concept: the microbiome can be regarded as a human organ from the physiological standpoint. Medicine has developed organ-based specialties such as nephrology, hepatology, cardiology or pneumology. Perhaps we can envisage ‘microbiomology’ as a future specialty of
or a branch of clinical microbiology, devoted to the study of the physiology, pathology, diagnostics, therapy and prevention of alterations of the community structure of the microbiome.

The human organism, like most living organisms, is the result of stable associations among cells of different origins and genetic lineages, from mitochondria inside the cells in the tissues to the microbiota attached to the surfaces of the human body, integrating members of all three domains of life on earth, Eukarya, Bacteria and Archaea, and their viruses. We are definitely not a ‘super-organism’ (a term with inappropriate Nietzschean reminiscences), but just a complex organism with a diversity of genetic compositions. Indeed the microbiota composition and its relation with the gut have resulted from the dynamics of selection and competition [1].

Organisms are identified by their ability to replicate in well-defined specific lineages. The ‘human lineage’ (human cells, including mitochondria) is obviously transmitted by vertical descent, but the human microbiota is also transmitted to the progeny in a less specific but highly reproducible way, thus giving rise to a consistent heritage of a common core microbiome with inter-personal variations maintained over generations within a kinship [2].

As the microbiome is a highly complex structure, involving several thousands of different bacterial taxonomic units and therefore millions of links between them, the question emerging is how this complexity can be inherited. Stanley Milgram (1933-1984), a social psychologist, was teaching a long time ago the concept of ‘small world’, illustrated by the ‘six degrees of separation’ thought experiment. Everyone is on average approximately only six steps away, by way of introduction, from any other person on Earth. This happens because there are important nodes (‘hubs’) in the relational network that help to find other nodes, and the access to each new node creates new possibilities of finding individuals, to a certain extent along a power law dynamics. The application of this concept (without literally taking into account ‘six steps’) to the rapid building-up of the extreme complexity of human microbiota is illustrated in Fig. 1. In humans, a number of ‘starting’ bacteria such as Lactobacillus, Prevotella or Sneathia might be acquired during vaginal delivery [3, 4] and possibly other pioneering populations are acquired by breast feeding [5]. It might be suggested that these early colonizers serve as sinks or attractors for other microbial partners (open curves in Fig. 1), and those for others thereafter; eventually pairs or higher
consortia of organisms create novel niches for other organisms. The corresponding law of attraction remains one of the most important items to be investigated in *microbiome* biology [5], but it might relate to genomic functional complementarity following genetic reductions, following a model proposed for bacteria-eukaryotic cell *coevolution* [6]. As in the ‘small world’ metaphor, a complex system can be constructed rapidly and specifically. Note that, as in an integrated puzzle, the same system can be constructed from different nodal origins.

1. Download full-size image

FIG. 1. ‘Small world’ hypothetical steps for the construction (reproduction) of *microbiota*. Upper part, left, a bacterial organism exposing ‘attractors’ (open curves) for other bacterial partners in the consortium; in the middle, the partners are present and themselves expose a variety of novel attractors, and the process progresses with a *power law* dynamics on the right. Lower part, the same schema applied to intestinal colonization; the host-attached pioneer population or community serves as attractor for other bacterial organisms circulating in the open system that are progressively inserted in the complex system.
As in other fields of medicine, pathology frequently reveals the physiology of a system by illustrating the consequences of alterations and deficiencies. The importance of the microbiome has been highlighted by the microbial ‘abnormalities’ found in pathological conditions such as inflammatory bowel diseases, obesity or malnutrition. Diagnosis of microbiome diseases is based at present on full metagenomic DNA sequencing and computational advances that can inform about and differentiate core microbiota and changing microbiota [7, 8]. These ‘diagnostic’ techniques should also be able to evaluate the role of mobile genetic elements, which deeply influence the connectivity of the microbiome [9, 10]. The therapy of microbiome diseases will be part of future interventions based on eco-evo drugs and strategies [11]. The use of prebiotics and probiotics to ‘equilibrate’ altered human microbiota represent rather empirical approaches which require much more basic and clinical research to advance on a scientific basis [12]. Addressing microbiome restoration by transplantation is crucial to advance in the curing of microbiome diseases. This approach has already been used, with very limited adverse effects, [13] for treating microbiome diseases such as Clostridium difficile associated pathologies, inflammatory bowel diseases, metabolic syndrome, obesity, neurodegenerative diseases and autoimmune and allergic diseases [4, 14, 15]. The possibility of engrafting new microbiota from a donor source [16] has been demonstrated. Fourteen days post-transplantation, the recipient microbiota was shown to be highly similar to the donor [17]. Progress in this field will be facilitated by using frozen preparations ready for transplantation [18] and experimental animal models [19]. Microbiota transplantation might also alter host resistance to infections [20]. A more advanced field of research in the therapy of microbiome diseases will be the discovery of drugs acting on host-microbiome and intra-microbiome signals and interactions [21]. However, we reiterate that little is known about the biochemical signals and micro-ecological structures assembling the different bacterial populations, and the bases for their maintenance and coordinate functionality [5]. The fascinating field of microbiome research has just started to yield knowledge of the multiple consequences of the alteration of the full microbial complement, a real organ, which is part of the human body. The relevance for human body and even human behavioural health will continue to be revealed in the years to come [2].
This research will stimulate integrative thinking to understand integrative complex structures and will importantly contribute to provide insights in a future ‘grammar of life’ research. Welcome to microbiomology!

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Transparency declaration

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Eclosion:
1. The Scientific Process of Becoming an Adult
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Candida in its yeast state makes Serotonin. Serotonin in the gut stops Candida from becoming Disease Causing Fungus – Another of Nature’s Elegant Feedback Loops

Serotonin and candida are unusually linked. The happiness hormone, Serotonin, is not something you expect to see connected to Candida albicans. It is something we talk about more in relationship to brain dysfunction and mood disorders. Serotonin and candida is something we don’t hear much about.

If we consider that 80-90% of the production of the body’s serotonin happens in the gastrointestinal tract, the distance between the two narrows significantly and a possible relationship between the two makes more sense.

Why the GI Tract produces so much serotonin is not completely known yet (motility and appetite are two effects), but a functional link between serotonin and candida has been established, and it’s not about serotonin making candida happy.

Scientists from Austria have shown that serotonin has anti-fungal activity against candida, helping to control its ability to change into its problematic fungal form and the activity of enzymes produced by it. Depending on the concentration of serotonin present, at lower concentrations, it can first interfere with the activity of candida’s enzymes, and at higher concentrations, it can significantly limit its fungal growth.

It has been shown that the bacteria of the intestinal tract play a role in the production of serotonin and since fungal candida effectively regulates and alters bacterial ratios in the gut after antibiotic use, just as serotonin affects it, it can affect serotonin. In short, gut bacteria regulate serotonin levels and candida regulates gut bacteria. Serotonin and candida are linked.

Also
Another factor is that fungal candida increases inflammation throughout the body and this has been shown to play a role in neurological conditions such as depression and anxiety.

Research from King’s College in London shows that inflammation is often linked to diabetes and depression. Researcher, Dr. Khalida Ismail states, “Inflammation may be driving a number of different long-term conditions. That’s quite a new way of thinking of the mind and the body”.

Fungal candida can also play a role in creating diabetes through its pro-inflammatory effects and the induction of the body’s TH-17 immune response. The creation of blood sugar imbalances is associated with depression and depressive behaviors.

These effects can once again be linked to an increase in brain inflammation associated with hypoglycemia and diabetes. Researchers at the University of Washington found that depression was “significantly associated with...hypoglycemia.”

Fungal candida is implicated in conditions such as MS, CFS, ME, arthritis, psoriasis, and other autoimmune diseases by researchers in Germany and Switzerland. The primary factor in the relationship between candida and depression, as well as a long list of other conditions, is inflammation.

**Antibiotics**

Many of these effects can be traced back to antibiotic use and it’s not the abuse of antibiotics, it’s the simple use of antibiotics. In killing 100 trillion bacteria in the body within 5 to 7 days, antibiotics cause a massive flooding of the body’s tissues with bacterial cell components that humans are highly allergic to.

This can prime the body and the brain for a lifetime of inflammation and disease. Fungal candida results from antibiotic use and drives a lot of inflammation in the body linking it to over 125 different conditions.

Of course, not all is lost and the body can be brought back into balance through the application of sound principles and an understanding of the body’s physiology and systems, microbiome, and fungal mechanics. Get started today on Dr. McCombs Candida Plan to re-experience a life of vitality!
When all else fails, remember to laugh, as laughter stimulates the release of serotonin, which in turn inhibits candida.

Other recent posts:

5 Mistakes To Avoid When Treating Candida
– https://www.candidaplan.com/5-mistakes-to-avoid-when-treating-candida/

5 More Mistakes To Avoid When Treating Candida
– https://www.candidaplan.com/5-mistakes-avoid-treating-candida/


Candida Auris: Striking Gold with Candida Auris

All hail reproducibility in microbiome research

- Jacques Ravel Email author and
- K Eric Wommack Email author

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At its core, microbiome research relies on complex and sophisticated statistical analyses of large datasets and their associated metadata (e.g., experimental parameters, sample characteristics). Heavy reliance on big data has presented new challenges in communicating the details of complex analyses in a manner sufficient for others to replicate analytical workflows. Reproducibility is a pillar of sound research, and scientific journals need to embrace transparency and make every effort
to enable reproducibility through comprehensive and clear reporting of analytical approaches. In this issue of Microbiome, a report by Meadow et al.\cite{1} on the microbial communities of classroom surfaces sets a new bar for thoroughness in the availability of data, metadata, and analytical resources (code and scripts). It is our hope that this paper will serve as a template for the clever use of publicly available resources and code repositories to enable fully reproducible microbiome research.

“Scientific publications have at least two goals: (i) to announce a result and (ii) to convince readers that the result is correct… papers in experimental science should describe the results and provide a clear enough protocol to allow successful repetition and extension” \cite{2}. Reproducibility and extension are only possible if: data is easily and freely accessible and delivered in format that adheres to international standards; and analysis workflows and scripts are embedded in the publication. Microbiome research is, by its nature, a multi-disciplinary endeavor where experimentalists often work with biostatisticians, mathematicians, computer scientists, or epidemiologists. At times, this multi-disciplinary character can result in a clash of scientific cultures with different approaches to openness, transparency and data release. For example, large sequence datasets and most importantly associated metadata have resulted from our work with epidemiologists \cite{3, 4}. However, the notion of releasing data and analysis scripts along with a publication has often been met with great surprise by our epidemiology colleagues. Now that microbiome research is transitioning from a descriptive and associative science to a translational science that will start impacting lives, we feel the time is right for the community to set standards for complete transparency and full reproducibility. Experimental science suffers each time there is a realization that a high profile report of a scientific finding is not reproducible. Over the long term, news stories of irreproducible science in the popular press can have lasting negative effects on the credibility of the scientific community in general \cite{5}. Without reproducibility, microbiome science will battle to regain credibility and opportunities for scientific advancement will be lost.

Scientific journals should be at the forefront of efforts to ensure that data is accessible prior to publication and made available during the peer review process. Today, fortunately, there are numerous options for data release, such as among others, the NCBI Database of Genotypes and Phenotypes (dbGaP - http://www.ncbi.nlm.nih.gov/gap) and the Short Read Archive (SRA - http://www.ncbi.nlm.nih.gov/sra/), options selected by the Human Microbiome Project for example, or other services such as FigShare (http://www.figshare.com), which was used in the Meadow et al paper \cite{1}. Data deposited into FigShare is permanently archived and redundantly backed up at major universities around the world through the CLOCKSS system (a not-for-profit venture started by libraries and publishers committed to ensuring long-term access to scholarly publications in digital format - http://www.clockss.org), and a permanent digital object identifier (DOI) is supplied with each dataset. Metadata associated with any dataset should also be made available, and in standard format with controlled ontology. Standards such as the minimum information about a marker gene sequence (MIMARKS) or the minimum
information about any (x) sequence (MIxS) [6] are community driven standards that if fully adopted would enhance the long-term scientific use of microbiome datasets.

Data availability is critical but detailed descriptions of the procedures used in the processing of raw data and statistical analyses are equally important for reproducibility. Simply providing scripts and workflow is not enough; data and code have to be understandable to be reproducible. Hence, commenting and versioning is essential and should be included in the publication of scripts. There are several tools available depending on the statistical package or programming language. For example, iPython notebook (http://www.ipython.org/ipython-doc/dev/interactive/notebook.html) for python scripts enables commenting and tutorials for documenting use cases. Popular tools such as DigiNorm developed by Dr. C. Titus Brown (Michigan State University) use iPython notebook (http://www.ged.msu.edu/papers/2012-diginorm/) and it is no mistake that the best documented tools often turn out to be more frequently used by microbiome researchers. Statistical analyses in microbiome research increasingly rely on the R statistical language [7]. The R Markdown language simplifies creation of fully-reproducible statistical analysis [8], and has been implemented in packages such as Sweave [9] or knitr [10]. Combined with GitHub (http://www.github.com), a code versioning repository, scripts can be run and analytical outcomes from reported datasets can be fully reproduced. Dozens of other packages are available for commenting and release of workflow and scripts. Again, Meadow and co-authors [1] used both knitr and GitHub in making their statistical workflow and code publicly available. We applaud the efforts of initiatives such as the Minimum Information About a Bioinformatics investigation (MIABi) [11], which seeks to advance standards for bioinformatics activities that will improve the persistence, reproducibility, and disambiguation of code. Ultimately, these practices will improve transparency and reproducibility. Moving forward Microbiome will seek to raise the bar for reproducibility in microbiome research by asking authors to provide easy access to data and code that will ultimately enrich our vibrant and growing research field.

Declarations

Competing interests

The authors declare that they have no competing interests.

Authors’ contribution

JR and KEW wrote the manuscript. Both authors read and approved the final manuscript.


10. Xie Y: knitr: a comprehensive tool for reproducible research in R. Implementing Reproducible Computational Research. Edited by: Stodden V,
Changes of the human gut microbiome induced by a fermented milk product

Patrick Veiga, Nicolas Pons, Anurag Agrawal, Raish Oozeer, Denis Guyonnet, Rémi Brazailles, Jean-Michel Faurie, Johan E. T. van Hylckama Vlieg, Lesley A. Houghton, Peter J. Whorwell, S. Dusko Ehrlich & Sean P. Kennedy

Scientific Reports volume4, Article number: 6328 (2014) | Download Citation

Abstract

The gut microbiota (GM) consists of resident commensals and transient microbes conveyed by the diet but little is known about the role of the latter on GM homeostasis. Here we show, by a conjunction of quantitative metagenomics, in silico genome reconstruction and metabolic modeling, that consumption of a fermented milk product containing dairy starters and Bifidobacterium animalis potentiates colonic short chain fatty acids production and decreases abundance of a pathobiont Bilophila wadsworthia compared to a milk product in subjects with irritable bowel syndrome (IBS, n = 28). The GM changes parallel improvement of IBS state, suggesting a role of the fermented milk bacteria in gut homeostasis. Our data challenge the view that microbes ingested with food have
little impact on the human GM functioning and rather provide support for beneficial health effects.

Introduction

The gut is inhabited by microbial communities that form an intimate and beneficial association with the host. It is an open microbial ecosystem composed of resident commensals that are continuously exposed to transient exogenous microbes originating from the diet. Many fermented foods and yoghurt in particular, contain high quantities of live bacteria, typically up to $10^9$ CFU/g. These foods have been major contributors to the human diet since the Neolithic Era, yet our modern understanding of the impact of food-ingested bacteria on our resident gut microbiome remains limited. To date, a majority of studies failed to identify significant modulations of the resident human gut microbiota upon consumption of fermented food. This is likely due to the use of methods lacking sufficient phylogenetic resolution at the species level.

During the last two decades, human gut microbiota structure has increasingly been assessed by culture-independent methods based on 16S rRNA gene quantification or sequencing. These methods can assess the overall structure of microbial communities but remain restricted in phylogenetic identification i) to the genus or species-subgroup levels and ii) by the availability of phylogenetically characterized 16S rDNA sequences in public databases. High throughput DNA sequencing-based approaches have emerged as a powerful alternative to study the complex microbial communities. This deep sequencing permitted the construction of the first human gut microbiota gene catalog. Subsequently, quantitative metagenomics has achieved species-level resolution, not only for previously known organisms but also for unknown species. These technical and analytical advances provide the tools to explore the composition and metabolic capacity of the microbiota with an accuracy heretofore unattainable.

We deployed and extended these advances to identify gut microbial species modulated by a fermented milk product (FMP) in a 4-week intervention study in subjects suffering from Irritable Bowel Syndrome (IBS) with constipation ($n = 28$). IBS is a chronic functional disorder of the intestine with a prevalence of 10% to 25% and where 67% of diagnoses are for women.

We aimed to use a species-level metagenomic approach to identify specific members of the gut microbiome modulated by the FMP. We found that the FMP potentiated the production of butyrate and others short chain fatty acids (SCFA) and decreased the levels of the opportunistic pathogen, *Bilophila wadsworthia*. These modifications occurred in parallel with an improvement of IBS symptoms. Metabolic reconstruction of known and unknown species suggests potential cross-
feeding involving the food-ingested bacteria and resident commensals that might be relevant for the overall gut homeostasis.

RESULTS We administered a FMP or an acidified milk product (MP; 125 g/serving) to subjects fulfilling the Rome III criteria for IBS with constipation (IBS-C) during 4 weeks (Figure 1). Bacteria contained in the FMP were Bifidobacterium animalis subsp. lactis CNCM I-2494, Streptococcus thermophilus CNCM I-1630 Lactobacillus delbrueckii subsp. bulgaricus CNCM I-1632 and CNCM I-1519 and Lactococcus lactis CNCM I-1631. The consumption of the FMP improved the IBS condition of the subjects compared to the control group (i.e. abdominal distension, acceleration of the oro-caecal and colonic transit times, overall IBS symptom severity) (Figure 1). In order to assess the impact of the FMP on the gut microbiota of the enrolled subjects, we collected their stools before and after the intervention, extracted and sequenced their fecal DNA using a SOLiD v4 Next Generation Sequencing (NGS) device. We compared the sequencing data against the human gut microbiome catalog of 3.3 million genes.

Figure 1: Study design and overview of the bioinformatic pipeline used in this study.

![Study design and bioinformatic pipeline](image-url)
Genes of FMP species are detected in fecal samples.

To validate the sensitivity of the method, we verified that DNA originating from the FMP bacterial species could be efficiently recovered in stool samples. We complemented the human microbiome catalog with 9030 non-redundant genes of the FMP genomes, otherwise absent, to insure an optimum mapping of the reads against the FMP genes. Abundance of all FMP species was significantly increased in stool samples in the FMP group at the end of the study. The low level signal detected at baseline and in control subjects is likely due to the presence of endogenous species phylogenetically close to the FMP species (Figure 2 A/B). B. lactis CNCM I-2494 was the dominant FMP species in stool, in agreement with its relatively high survival in the upper GI tract19,20.

Figure 2: The FMP and MP modulate species of the gut microbiota.
(A,B) Relative abundance of the FMP-species measured in FMP (A) and MP (B) groups at baseline and after intervention. (C,D) Relative abundance of known or unknown (MGS) species measured in FMP (C) or MP (D) groups at baseline and after intervention. Only MGS that were significantly modulated are depicted. Statistical significance is reported by asteriks (*:p<0.05, **:p<0.001; Wilcoxon-paired test corrected for multiple tests comparison using the Benjamini-Hochberg procedure). Results are presented using Tukey box-and-whisker plots as quartiles (25%, median, and 75%). Outliers were illustrated as single dots as per Tukey option of the Prism Graph software.

Endogenous microbial species are modulated by the FMP

Starting from a comprehensive gene-centric approach, we aimed to reduce data complexity from whole genome sequencing (WGS) reads to individual species. Our bioinformatics pipeline, summarized in figures 1 and S1, relied on 2 key principles: i) Increase (decrease) of a species results in enrichment (deprivation) of the abundance of its genes in the fecal microbiome. Consequently, gene counts should lead to identification of species modulated by the intervention. ii) Genes of a single species should have similar co-abundance profiles across individuals since they are physically linked on a DNA molecule (chromosome, plasmid, phage). As a result co-abundance based gene-clustering leads to identification of clusters of genes corresponding to one bacterial species as already demonstrated14,15.

We identified 1320 and 641 genes as significantly over- or under-represented after the consumption of the FMP or milk product (MP), respectively. We designated these FMP or MP “modulated genes”. Twenty seven percent of the FMP-modulated and 22% of the MP-modulated genes could be assigned to known species by blastN (Figure S2 A/B/C). Clustering by Spearman correlation was applied to the 1320 and 641 modulated genes using the MetaHIT cohort to increase statistical power and improve species assignment36.

Benchmarking against genes assigned to known species revealed that for clusters retrieved with a Spearman correlation factor of 0.75, 97% of genes were assigned to one cognate genome (i.e. known species) (Figure S3). This result confirms that clusters of genes identified can accurately serve as a proxy for intestinal bacterial species. Our analysis revealed that three clusters of modulated genes were derived from known species: Bilophila wadsworthia, Parabacteroides distasonis and Haemophilus parainfluenzae. Eleven additional clusters of genes without species-level identities were retrieved from the 1961 modulated genes (Figure S2D/E). The assignment of genes to unknown species allowed us to increase the percentage of genes without species-level identities for the FMP group from 27% to 51% (Figure S2A). Unknown species were assigned a number prefixed with the tag “MGS,” for MetaGenomic Species.
Integrating both known species and MGS results in a significant gain in statistical power through the compression of the number of variables as compared with the full catalog of 3.3 million genes. The identification of co-variant clusters also yields signatures that are more reliable than a single gene target. We computed the relative abundance of each known or unknown species by averaging the frequency of 50 representative genes for each species, as reported previously and compared the abundances using a Wilcoxon paired-test corrected for multiple testing. This revealed that consumption of the FMP stimulated MGS126, MGS203, MGS106, MGS109 and Bifidobacterium dentium. Three species, Parabacteroides distasonis, B. wadsworthia and Clostridium sp. HGF_2 were found to be inhibited (p<0.05) (Figure 2C). In the MP group, only two species, Haemophilus parainfluenzae and MGS204 varied significantly (p<0.05) (Figure 2D).

Reconstitution of the genetic repertoire of unknown species

We then attempted to extend the co-variance approach to the full catalog of 3.3 million genes in order to retrieve other genes of the FMP or MP modulated species. A unique gene of a given cluster was used as a “prey” to “chase” the genes of the catalog co-varying with the prey at a given threshold. Sets of co-varying genes from the full catalog were retrieved in a step by step approach, and formed metagenomics clusters centered around the initial modulated genes identified above. We benchmarked this approach with 10 known species (Table S1), and retrieved an average of 2554 genes per species with a specificity of >95%, illustrating the applicability of this approach for retrieving genes of unique bacterial species (Table S1, cf. supplementary material). We applied the same procedure to the FMP-modulated MGS and retrieved >1900 genes for all the MGS (Figure S5A) but 2 (MGS106, MGS109), which had sub-bacteria-sized gene repertoires and were not further investigated. Five MGS were identified as Clostridiales including Eubacterium (MGS146), Clostridium (MGS134), Roseburia (MGS204) and unknown genera (MGS203, MGS126) and 2 MGS as Bifidobacterium(MGS109, MGS106) (Table 1, Supplementary Material).

Table 1: Taxonomic assignment of unknown species (MGS)

The genetic repertoire of a MGS should contain the information needed to perform essential bacterial functions (e.g. DNA replication, peptidoglycan synthesis, protein synthesis). Essential genes represented an average 9.5% of MGS genetic repertoires, which is comparable to other gut commensals such as Escherichia coli and Bifidobacterium longum (Figure S5B). By the same token, it is expected that functions encoded by MGS should also cover the major metabolic pathways present in any microbial cell (i.e. carbohydrate, lipid, amino acids and nucleic acids metabolisms). Genes of MGS were assigned putative functions by comparing them to Cluster of Orthologous Groups (COGs) using the CD-Search Tool. Sorting of these COGs by their hierarchical functional categories confirmed that functions...
encoded by the MGS similarly cover the major metabolic pathways compared to reference commensals (*E. coli* and *B. longum*) (Figure S5C). This result was supported by the projection of the MGS and *E. coli* on the global map of KEGG metabolism (Figure 3A, Figure S6).

Figure 3: Metabolic reconstruction of unknown gut microbial species shows a FMP-mediated increase of potential butyrate producers.

A) Projection on KEGG metabolic pathways of functions encoded by the MGS126 reconstructed genome (in red) using Ipath tool. Functions of the KEGG global map were depicted underneath. B) Presence of genes

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22: *Faecalibacterium prausnitzii*
35: *Lachnospiraceae bacterium S_1_63FAA*
3: *Coprococcus ART55/1*
30: *Eubacterium hallii*

12: MGS126
1: *Roseburia intestinalis*
19: *Clostridium sp. L2-50*
4: *Roseburia inulinivorans*

17: *Butyrivibrio cossatus*
121: *Aclidamicrobium sp. D21*
44: MGS203
20: MGS204
predicted to encode enzymes of the butyrate synthesis pathway (thiolase EC 2.3.1.9 (THL); β-hydroxybutyryl-CoA dehydrogenase (BHCD; EC 1.1.1.35); crotonase (CRO; EC 4.2.1.17); butyryl-CoA dehydrogenase (BCD; EC 1.3.99.2); Electron-Transfer Flavoprotein α and β sub-units (ETFα and ETF β; E.C. 1.5.5.1); butyrate kinase (BK; EC 2.7.2.7); butyryl-coA acetyl-coA transferase (ButCoA; EC 2.8.3.8) among the reconstituted Clostridiales MGS. C) Abundance of butyrogenic modules of the human gut microbiota in the IBS cohort at baseline. Mean and standard deviation are represented. Results are presented using Tukey box-and-whisker plots.

We concluded that we retrieved nearly complete genomes of the FMP-modulated species, allowing further metabolic and ecological analyses.

FMP increases potential butyrate producers

The Clostridiales are primary butyrate producers. Our analysis revealed that MGS126, MGS203, MGS204 and Clostridium sp. HGF2 possess the genetic capacity to produce butyrate (Figure 3B). In order to assess the impact of the FMP on the butyrate producing community, we reconstituted the butyrogenic modules of the entire human microbiome gene catalog by applying the gene-clustering algorithm to the genes of the catalog encoding the butyrate synthesis pathway (cf. Supplementary Methods). This procedure yielded 39 butyrogenic modules of which 30 could not be taxonomically assigned at the species level (Figure 3C). The 9 species-assigned modules were previously reported to belong to experimentally-confirmed butyrate producers Roseburia intestinalis, Roseburia inulinivorans, Butyriovibrio crosstus, Clostridium L2-50, Faecalibacterium prausnitzii, Eubacterium hallii, Lachnospiraceae bacterium 5_1_63FAA, Coprococcus ART55/1 and Acidaminococcus intestini D21. Among the 30 non-assigned species modules, 27 belong to the Order Clostridiales including 5 Lachnospiraceae, 8 Clostridiaceae, 2 Veillonellaceae and 1 Bacteroidales. Each of these taxa is known to have members capable of butyrate production. This result validated our approach, as we retrieved butyrogenic modules belonging to major known intestinal butyrate producers. The relative abundances of the butyrogenic modules were calculated across the studied cohort. Module 12, among the 10 most abundant, belongs to MGS126. Modules 44 and 20 belong to MGS203 and MGS204, respectively. As expected, in parallel with their respective MGS, modules 12 and 20 were significantly increased and decreased after FMP and MP consumption, respectively (Wilcoxon paired test; data not shown). A trend (p<0.10) showing an increase of the module 44 (MGS203) was also observed in the FMP group, although it did not reach statistical significance (data not shown). Intergroup comparisons of butyrogenic modules after the interventions indicated a higher abundance of module
Butyrogenic bacteria are known to produce propionate as an end product of L-fucose degradation. The presence of L-fucose degrading genes in the genomes of MGS126 and MGS203 might indicate a metabolic potential to also produce propionate (Table 2).

Table 2: Selected shared functions of FMP-modulated species

FMP stimulates the production of SCFA in vitro

In order to further assess the impact of the FMP on short chain fatty acid production we used a 5-compartment ex vivo human colonic fermenter (SHIME ® PRODIGEST) inoculated independently with 2 different healthy donors and kept stable for >5 weeks. We observed that the addition of the FMP led to a significant increase of butyrate, propionate and total SCFA, in the 3 different vessels mimicking the ascending, transverse and descending colon conditions as compared with baseline (Figure 4, Figure S7). Butyrate was the SCFA with the largest observed increased registering an average 1.9 fold augmentation across vessels and individuals (Figure 4).
week (C1 & C2 time points) exposed to FMP during 3 weeks (T1, T2 and T3 time points). Mean fold changes between control and treatment periods are reported when statistical significance was met. n.s: non-significant, *** (p<0.001, ANOVA).

Functions encoded by FMP-modulated bacteria

Next, we reasoned that species stimulated (or decreased) by the FMP might have responded to the same environmental intraluminal changes triggered by the ingestion of FMP bacteria. We aimed to have a better insight on habitat type, cell cycle and energy metabolism of the FMP modulated species by identifying shared functions of FMP-stimulated species absent in FMP-inhibited species, and vice-versa. Available genome information of known species and the reconstituted genetic repertoires of MGS were used to perform comparative genomics and identify Clusters of Orthologous Genes (COGs)21 discriminating between FMP-stimulated and inhibited species (Table 2, TableS2).

Genes encoding pili were present in all FMP-modulated species indicating a potential for epithelial adhesion. MGS126 and MGS203 possessed enzymes allowing utilization of L-fucose which is a mucin derived monosaccharide. These 2 species also carried genes encoding the syntheses of flagellin and spores, which have both been reported to be involved in mucus colonization31,32. Taken together, this data informed us on the possible adaptation of these species to a mucous environment.

The presence of genes involved in oxidative phosphorylation (i.e. cytochrome oxidases bd) in B. wadsworthia and P. distasonis genomes indicates a shared capacity of these species to inhabit niches where oxygen tension is low (i.e. epithelial interface).

We further investigated whether inhibited species shared common features that would be absent in stimulated species. Genes encoding a putative carbon monoxide dehydrogenase (CODH) were found to be present in B. wadsworthia and Clostridium sp. HGF2 genomes predicting their capacity to use carbon monoxide (CO) as an electron donor33. Heme oxygenase is a known source of intestinal CO and its activity has been shown to be up-regulated during intestinal inflammation34. This suggests that CO utilization might be an advantage in inflamed conditions for organisms able to use it. B. wadsworthia also possesses the set of genes (i.e. HMP0179_00240-00243) allowing anaerobic respiration of nitrate, a substrate that is also enriched during inflammation35.

Discussion
Fermented foods have been a part of the human diet since ~10 000 BC comprising different matrixes such as milk (i.e. kefir, yoghurt, dahi, cheese) or vegetables (i.e. nato, sauerkraut, pickles). Beneficial effects of fermented milks were empirically assessed by the Nobel Prize laureate Elie Metchnikoff in 1907 who predicted their role in the enhanced health and longevity of Bulgarian populations. In the light of our increased understanding of the impact of the gut microbiome on host health, the question arises how food-ingested microbial communities modulate the autochtonous microbiota.

The emergence of molecular tools based on the 16S rDNA gene brought about a revolution in understanding the immense diversity of gut microbial communities and their links with host health and diet. However, variations of 16S rDNA sequences do not provide basis for species-level resolution. Consequently, studies using 16S gene as a phylogenetic marker and reporting unaltered gut microbiota upon probiotic consumption might have failed in detecting changes of the microbiota due to the lack of species-level resolution. Such hypothesis can be accurately studied now with the emergence of novel technologies allowing species-level gut microbiota mapping.

In the current work, whole genome sequencing analysis coupled with a gene-centric approach was used to investigate the effect of a FMP on the human gut microbiota at the species-level resolution. Initially, only 27% (356 of 1320) of genes modulated by the FMP could be assigned to known species; illustrating the limited representation of bacterial commensals in publicly available genome databases. By employing gene clustering methodologies, the species-level assignment of FMP-modulated genes was increased to 51%. This clustering algorithm was further used to reconstitute the bacterial gene repertoires of the unknown species used for comparative genomics.

Upon FMP consumption, two previously uncharacterized butyrate producers MGS203 and MGS126 were increased. MGS126 was among the 10 most abundant butyrogenic bacteria of the human gut microbiota. This argues for a positive effect of the FMP on the net production of butyrate in the colon. Importantly, this hypothesis was supported by our in vitro results obtained with the SHIME® fermenter and in a mouse model of intestinal inflammation. MGS203 and MGS126 were likely stimulated by the FMP-mediated increase of Bifidobacterium species resulting in a higher production of acetate and lactate, used by butyrate producers.

Recent studies have shown that B. wadsworthia and P. distasonis were increased in western diet enriched in saturated animal fat or RS4, a resistant starch used in processed foods, respectively.
Although an unlikely potential effect of dietary changes between groups cannot be excluded to explain the decrease of these 2 species in the FMP group, we privileged the more likely hypothesis that the FMP modulated-species responded to FMP-mediated signals. We thus reasoned that species inhibited in the FMP group shared common metabolic pathways that we investigated by comparative genomics.

_B. wadsworthia_ is a gram negative δ-Proteobacteria first isolated from an appendicitis patient and is often associated with inflamed and/or infected clinical samples. Its genetic potential to utilize the known inflammation-associated metabolites like nitrate and possibly carbon monoxide, suggests that it can be fueled by host-derived products enriched during inflammation, similarly to other pathobionts (i.e. _Salmonella enterica_). By the same token, the carbon monoxide dehydrogenase genes of another FMP-modulated species, _Clostridium_. HGF_2_, suggests that it could also take advantage of intestinal inflammation. Both _B. wadsworthia_ and _Clostridium sp. HGF_2_ are decreased by the FMP, which could thus have an anti-inflammatory effect as observed in the mouse model of colitis.

The FMP-induced changes in the GM paralleled improvement of IBS condition in our cohort, suggesting a role of the FMP-modulated species in the amelioration of the clinical parameters. This hypothesis is compatible with the observations that i) butyrate, known to improve intestinal motility and visceral sensitivity, is underproduced by IBS-C gut microbiota compared to healthy controls and ii) _B. wadsworthia_ is pro-inflammatory and produces sulfide which is toxic and nociceptive.

The MP has reduced effects on gut microbiota compared to the FMP which is consistent with the absence of an active microbial community in this product. Only 2 species, _H. parainfluenzae_ and the Clostridiales MGS204, were shown to be modulated (i.e. decreased) upon the MP intervention. Changes observed in the MP group might originate from a natural variation of the gut community reported to be higher in IBS compared to healthy controls. Alternatively, it is also possible that the MP induced changes in the gut microbiota. Since _H. parainfluenzae_ is αγ-proteobacteria considered as a gut pathogen and previously associated with IBS in children, MP-mediated changes might therefore account for the reported MP placebo effect.

In conclusion, our study sheds light on the potential of the bacteria conveyed by fermented milks to stimulate synthesis of beneficial metabolites and decrease abundance of pathobionts. These modifications can potentially improve health and are thus of importance for public health recommendations in western countries. It indicates that the role of food-ingested bacteria in gut homeostasis has been underestimated, possibly because of methodological limitations that can, today, be overcome. Elucidation of the intricate links between food ingested microbes and human symbionts can thus be addressed.
Methods

Subjects and study design

The study was a single centre, randomized, double-blind, controlled, parallel-group design including women (aged 20–69 years), fulfilling the Rome III criteria for IBS-C. Subjects were asked to not consume probiotic-containing products or fermented dairy products. There was no dietary record. After an 11-day wash-out period, 32 subjects (Per Protocol) consumed (125 g/serving) twice a day either the FMP (n = 17) or an acidified milk product (MP) (n = 15) for 4 weeks. Out of 64 stools collected within the PP population, 56 samples (n = 26 and 30, for FMP and MP, respectively) passed DNA quality control and were used for further analyses. Other dairy products and probiotics were excluded from the diet.

Study products

The FMP contained $1.25 \times 10^{10}$ colony forming units per serving (cfu/serving) *Bifidobacterium animalis* subsp. *lactis* (strain number I-2494 in the French National Collection of Cultures of Micro-organisms (CNCM), Paris, France), $1.2 \times 10^9$ cfu/serving of *Streptococcus thermophilus* (CNCM I-1630) *Lactobacillus delbrueckii* subsp. *bulgaricus* (CNCM I-1632 and CNCM I-1519) and *Lactococcus lactis* (CNCM I-1631). The MP was an acidified milk product with low lactose content. FMP and MP were provided by Danone Research (Palaiseau, France).

Stool collection, storage, fecal DNA extraction and sequencing

Stool samples were collected before and after the 4-week consumption period. Immediately after defecation, a fecal sample was collected and stored in RNA*Later* solution (Ambion). The fecal suspension was homogenized and the volume of RNA*Later* was adjusted to achieve a final fecal dilution of 1:10 (wt/vol). 200 µl of the 10-fold dilution were added to 1 ml of Phosphate Buffered Saline (Sigma-Aldrich) and centrifuged for 5 min at 5,000 × g. The supernatant was discarded and the fecal pellet stored at −80°C. Fecal DNA was extracted as previously described. DNA samples were sequenced on a SOLiD v4 NGS (Life Technologies) following the standard protocol for fragment libraries. The raw SOLiD read data was deposited in the EBI European Nucleotide Archive under the accession number PRJEB7171.

Identification of the species modulated by the interventions

Our bioinformatics pipeline, summarized in the Figure S1, aimed to decrease data complexity starting from reads and identify bacterial species modulated by the intervention. In brief, 50-bases tags (reads) were generated with SOLiD v4 sequencer, mapped on the MetaHIT 3.3 million genes catalog and genes count profiles were generated for each individual. Genes potentially modulated upon the intervention (intra-group analysis) were identified with a Kruskall-Wallis test,
clustered and assigned to known or unknown species. Relative abundance of a given species was computed by averaging the frequency of 50 genes belonging to the species. DNA from the samples (n = 28) was sequenced with a SOLiD v4 sequencer and an average of 3.97 × 10^7 50-bases tags (reads) per sample were generated and mapped on the MetaHIT 3.3 million genes catalog (average 1.71 × 10^7 reads/sample; S.D. +/- 7.79 × 10^6). Only those tags that mapped uniquely (univocally) to a single gene and to the exclusion of FMP genomes were retained (1.30 × 10^7 reads/sample; S.D. +/- 5.88 × 10^6). To quantify FMP species, the catalog of 3.3 million genes was complemented by the non-redundant genes (n = 9030) of the FMP genomes. Genes count profiles were generated for each individual and genes significantly enriched or depleted upon the intervention (intra-group analysis) were identified with a Kruskall-Wallis test. Clusters of genes or species counting less than 9 (or 5) genes in the FMP (or MP) group were disregarded since these clusters are more likely to have resulted from random variations (see supplementary material).

Quantification of mapped reads to the annotated reference was used to identify genes belonging to the endogenous microbiota that were significantly modulated upon intervention. A Mann-Whitney test was performed for FMP and MP groups to identify genes over or under represented after intervention compared to baseline. These are subsequently referred to as “modulated genes.” 1320 and 641 modulated genes were identified for FMP and MP, respectively.

Spearman correlation coefficients were calculated for all gene pairs of this set, using gene abundance as a variable. Clusters of genes were defined as co-varying gene groups at 0.75 spearman correlation threshold. To augment the statistical power of the clustering analysis, we used the gene abundance matrix of 292 individuals from the MetaHIT consortium (Metahit cohort). Genes were assigned to a species at a threshold of 95% identity over 90% of the sequence by blastN.

The genetic repertoire of unknown species was reconstituted through comparison of this study’s gene clusters and the co-variation within the 3.3 million gene catalog across the MetaHIT cohort. Functions for each clustered or reference genome genes were predicted using COG and/or NOG assignments. When available, COG assignment was performed using the Batch Web CD-Search online tool (http://www.ncbi.nlm.nih.gov/Structure/bwrpsb/bwrpsb.cgi). Predicted functions were projected on KEGG metabolic pathways using the Ipath software and compared to essential genes identified in the model organism Bacillus subtilis. When species-level taxonomy could not be assigned, higher taxonomic levels were assigned using MEGAN. Relative abundance was computed as the average frequency of 50 randomly selected genes of a species. Wilcoxon paired test, corrected for multiple tests by the Benjamini-Hochberg procedure, was used to test the significance of the FMP or MP effects.
Butyrate producers of the human gut microbiome

Genes involved in butyrate production from *Roseburia intestinalis* or *Coprococcus eutactus* were used as references to retrieve homologs present in the human gut microbiome catalog by using a bi-directional BlastP. Such genes were re-organized into co-varying clusters, hereafter called butyrate modules, which belong to unique species ([supplementary material](#)). Relative abundance of the butyrate modules was calculated as the mean of the relative abundance of the genes composing the module. Wilcoxon paired test was used to test the statistical significance of the variation upon interventions (intragroup analysis). For intergroup comparisons, a one-way ANCOVA (Analysis of Co-Variance) was used on the change from baseline for each butyrate module with the group as factor. The relative abundance at baseline was considered as covariate. A Benjamini-Hochberg multiple testing correction was applied to control the False Discovery Rate.

FMP increases SCFA production in an *in vitro* colonic fermentation system

*In vitro* colonic fermentation model (SHIME® (Prodigest, Belgium)) mimicking the adult gastro-intestinal tract was used to assess the impact of FMP on production of gut microbial derived SCFA. The system was inoculated with fecal sample from healthy adults (*n* = 2). After two-week stabilization period, 50 g of FMP was added daily to the stomach compartment during 3 weeks. The 3 vessels mimicking the ascending, transveral and descending colons were sampled 3 times a week.

Concentrations of acetic acid, propionic acid, butyric acid were measured by liquid gas chromatography. A two-way ANOVA (Analysis of Variance) was used to evaluate the impact of FMP consumption on the production of SCFA. The first factor was the period of treatment and the second was the week of sampling nested in the period treatment. Tukey-Kramer post-hoc tests were used to determine which comparisons were significantly different if needed. Normality of residuals and homogeneity of variance were checked to validate ANOVA hypothesis. When the hypothesis of homogeneity of variance between groups was violated, the variance by week was used instead of a pooled variance to allow the use of ANOVA.

### References


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34.


Every major life activity depends on Oxygen. Oxygen is life. Oxygen destroys harmful bacteria in your body without affecting beneficial bacteria. Poor oxygen levels favour yeast infections. Almost everybody is affected by chronic low oxygen levels due to lifestyle and environmental issues.

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The gut microbiome is a vast community of trillions of bacteria and fungi inhabit every nook and cranny of your gastrointestinal tract, and have a major influence on your metabolism, body weight, propensity to illness, immune system, appetite and mood. These microbes mostly live in your lower intestine (the colon) and outnumber all the other cells in your body put together. Conceptually, we should view them as a newly discovered organ, weighing slightly more than our brains and nearly as vital. There are some organs we can live without, including our spleen, gall bladder, tonsils and appendix, but we wouldn’t survive long without our gut microbes. Intriguingly, no two microbiomes are the same – we are all unique. And more than ever, we’re finding out just how important these microbes are.

According to research, the richer and more diverse the community of microbes is in your gut, the lower your risk of disease and allergies. This has been shown in animal tests and also in human studies comparing the microbes of people with and without particular diseases. Examples from recent work at King’s College London include studies of diabetes, obesity, allergy and inflammatory diseases like colitis and arthritis. Meanwhile, there is mounting evidence that babies born via caesarean section miss out on some of the microbes they would obtain through a vaginal birth, which may make them more vulnerable to obesity, allergies and asthma.

So how can you increase the good bacteria in your body and give your microbiome a healthy boost? Here are some tips to get your gut going:

1. Increase your fibre intake

Aim for more than 40g per day, which is about double the current averages. Fibre intake has been shown to reduce heart disease and some cancers, as well as reduce weight gain.

2. Eat as many types of fruit and veg as possible, and try to eat seasonally

The variety may be as important as the quantities, as the chemicals and types of fibre will vary, and each support different microbial species.
Pick high-fibre vegetables

Good examples are artichokes, leeks, onions and garlic, which all contain high levels of inulin (a prebiotic fibre). Some vegetables like lettuce have little fibre or nutrient value.

Choose food and drinks with high levels of polyphenols

Polyphenols are antioxidants that act as fuel for microbes. Examples are nuts, seeds, berries, olive oil, brassicas, coffee and tea – especially green tea.

Avoid snacking

Also, try to increase intervals between meals to give your microbes a rest. Occasionally skip meals or have an extended fast – this seems to reduce weight gain.

Eat plenty of fermented foods containing live microbes

Good choices are unsweetened yoghurt; kefir, which is a sour milk drink with five times as many microbes as yoghurt; raw milk cheeses; sauerkraut; kimchi, a Korean dish made from garlic, cabbage and chilli; and soybean-based products such as soy sauce, tempeh and natto.
Drink a bit of alcohol

In small quantities, alcohol has been shown to increase your gut diversity, but large amounts are harmful to your microbes and your health.

Steer clear of artificial sweeteners like aspartame, sucralose and saccharine

These disrupt the metabolism of microbes and reduce gut diversity – in animal studies this has led to obesity and diabetes. Ditch the processed foods too, as these also upset microbes’ metabolism.

Spend more time in the countryside

People living in rural areas have better microbes than city-dwellers. While you’re at it, dust off your trowel: gardening and other outdoor activities are good for your microbiome.

Stroke animals

Studies have shown that people living with dogs have more microbial diversity.

Avoid antibiotics and non-essential medicines

Antibiotics destroy good and bad microbes, and it can take weeks to recover, so don’t take them unless you need them. Their use is also associated with obesity and allergies in animals. Even common medications like paracetamol and antacids can interfere with microbes.

Don’t be hygiene obsessed

Fastidious washing and overuse of antibacterial sprays may not be good for your gut.

Spend time close to a lean person

Studies in mice have shown that leanness may be contagious. Microbes from a lean animal can reverse obesity in a fat one, but strangely, obesity microbes are harder to transmit than lean ones.
Avoid food and vitamin supplements

Only a tiny proportion of supplements have been shown to be beneficial. Instead, focus on eating a diverse range of real food to get all your nutrients.

Eat like the Hadza

Hadza hunt for food using traditional bows and arrows. Here, they've killed several vervet monkeys © Getty

The Hadza people of Tanzania have a gut microbiome diversity that is one of the richest on the planet and about 40 per cent higher than the average American and about 30 per cent higher than the average Brit. The average Hadza person eats around 600 species of plants and animals in a year and has huge seasonal variation. They have virtually none of the common Western diseases such as obesity, allergies, heart disease and cancer. In contrast, most Westerners have fewer than 50 species in their diet and are facing an epidemic of illness and obesity.

You can find out more about my experience with the Hadza in issue 315 of BBC Focus.
A healthy gut is the cornerstone of a healthy body: when your gut microbiome is balanced and diverse, almost every other system in your body benefits. Similarly, an unbalanced gut can wreak havoc on everything from your metabolism to your mood. What you eat plays a huge role in the health of your gut. Supporting your gut with good bacteria from certain foods and taking a probiotic supplement is essential.

A damaged gut can lead to all sorts of digestive health issues including irritable bowel syndrome (IBS), SIBO, Crohn’s Disease, irregularity, stomach pain, bloating, and more.

One of the best ways to support your gut health is to eat well. Here are 13 foods with the highest potential to damage or disrupt your gut microbiome—and therefore avoid—followed by some foods you can eat to support a better gut health diet.

## Foods to Avoid in a Gut Health Diet

### Sugar

Refined white sugar may have a particularly bad reputation, but it turns out that sugar in any of its forms is potentially harmful to your gut health. Participants in a study of sugar’s effects on digestion reported increased constipation and poorer overall gut function while on a high-sugar diet. (1) Read our post on how to stop sugar cravings if saying no to sugar is a particular challenge for you.

### Processed Foods

Most of us know that processed foods aren’t exactly healthy, but the effects that they can have on your digestive system balance might surprise you. A recent study conducted on mice revealed that the emulsifiers used in heavily-processed foods disturbed their gut microbiota so much that many developed colitis and metabolic diseases. (2)

### Synthetic Chemical Food Additives + Sweeteners

These Un-Natural Patented chemicals feed the bad bacteria and make mental health impossible.

### GMO or Processed Soy

While sugar and processed foods are generally regarded as unhealthy, soy is often thought of as nutritious and beneficial. However, the high levels of processing that much of today’s soy goes through have changed how it affects the body. In fact, high levels of soy in your

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(1) [Study](#)

(2) [Study](#)
diet can have damaging effects on your gut microbiome as the ingredient has been shown to reduce key Bifidobacteria and Lactobacillus populations, two strains that are crucial for a balanced gut. (3)

Dairy

Even if you aren’t lactose intolerant, dairy may not be the best choice for your stomach. Studies have shown that dairy consumption changes the bacterial makeup of your gut within days, allowing strains linked to intestinal disease and inflammation to flourish. (4)

Red Meat

Like dairy, eating red meat can encourage the growth of certain bacterial strains that can negatively impact your health, from your weight to your immune function to your emotional state. The same study that found dairy to be problematic showed that red meat had the same ill effects on study participants’ gut microbiomes.

Gluten

Gluten—a protein found in a number of grains such as wheat and barley—has gotten a bad rap in recent years, and it turns out this reputation is unfortunately well-earned. While those with Celiac disease are particularly susceptible to its effects, studies have found that gluten can lead to stomach pain, bloating, and fatigue even in those without the disease. (5) Research has also indicated that going gluten-free lowers insulin resistance, inflammation, and weight gain/obesity. (6)

Eggs

While concerns about eggs raising bad cholesterol levels may have been debunked, new research indicates that eating eggs may lead to heart disease in a different way. Cleveland Clinic researchers found that a certain protein in eggs encourages the growth of gut bacteria that produce a chemical compound that causes clotting and thus raises the risk of heart attack and stroke. (7)

Genetically-Modified Organisms (GMOs)

In an effort to cultivate crops that are naturally resistant to pests and disease, scientists have created what is known as genetically-modified organisms (or GMOs); wheat, soybeans, and corn are the three most common GMOs in the United States. Unfortunately, the traits that help GMOs resist disease can have terrible effects on gut health: studies have found that consumption of GMO foods can reduce the beneficial bacteria populations in the gut. (8)
Excess Corn or GMO Corn

The reason that corn can be so detrimental to your gut health is simple: almost 90% of all corn grown in the United States is genetically modified. (9) The prevalence of corn in the American diet—and the general fuzziness surrounding what is and isn’t genetically modified—suggests that avoiding corn altogether might be the best choice for your gut health.

Farmed Fish

While the taste and availability of farmed fish and wild fish differ greatly, one major distinction between the two explains why farmed fish can be bad for your gut: the use of antibiotics in aquaculture. Huge amounts of antibiotics are included in the food that farmed fish are fed, and evidence suggests that these antibiotics can be passed along when these fish are eaten. (10) Of course, any antibiotic kills the healthy bacteria in your gut along with the bad bacteria, leading to an unhealthy balance of key strains.

Nightshades

Plants in the nightshade family such as tomatoes, eggplant, potatoes, and bell peppers are generally thought to be an important part of a healthy diet, but one key ingredient in all of these foods has the potential to cause serious gut issues. Naturally-occurring glycoalkaloids found in all nightshades have been shown to lead to intestinal inflammation and the condition known as “leaky gut” in mice, raising concerns about their effects on the human digestive tract. (11)

Tap Water

Staying hydrated by drinking enough water is obviously necessary, but you should be careful about the source of the water you drink. The water that comes from your tap is treated with a host of chemicals including chlorine, and research has found that chlorinated water can alter gut microbiota and even lead to the development of colorectal cancer. (12) Filtered water is the best option.

Artificial Sweeteners

Many people trying to lose weight turn to artificial sweeteners; after all, what could be bad about these zero-calorie treats? Quite a lot, as it turns out. Research increasingly points to a host of negative gut effects caused by artificial sweeteners, including changes to the gut microbial composition, increased glucose intolerance and higher rates of metabolic disease. (13)
Good Foods for a Gut Health Diet

After reading that list, you might feel a bit overwhelmed. Of course, avoiding all of these ingredients all the time is practically impossible, particularly if you enjoy a good pizza or bowl of ice cream every now and then. However, taking steps to reduce your intake of these foods and adding in a daily probiotic supplement to help preserve your beneficial gut bacteria can go a long way towards a healthier gut.

To help you transition to a more gut-healthy diet here are some foods you can consume more of as you begin to decrease your intake of those mentioned above.

Fiber-Rich Foods

Keep in mind, the good bacteria in your gut are living organisms. That means like any other living organism, they need food to survive and thrive. High-fiber foods are great for your gut health because they provide this sustenance for the probiotic bacteria in the form of prebiotic fiber. Read our post on prebiotics and why they are important to learn more.

Foods With Inulin

Inulin is a prebiotic fiber, meaning it feeds your good bacteria, promoting healthy gut flora. Because inulin cannot be broken down in your small intestines, it is able to make its way to your lower GI tract where your gut lives.

Foods with inulin include:

- Asparagus
- Chicory root
- Garlic
- Jerusalem artichoke
- Jicama
- Onions
- Yacon root

While these inulin-rich foods all provide prebiotic fuel for your gut bacteria, they also offer a number of other health benefits including constipation relief, weight loss, and balance blood sugar levels (helpful in managing Diabetes). (14)

Fermented Foods

Fermented foods including sauerkraut, kimchi—a Korean version of sauerkraut, kombucha, tempeh, and miso are beneficial for the gut because they have probiotics from the
fermentation process. Regarding miso, you want to choose unpasteurized since the pasteurization process kills much of the naturally-occurring probiotic bacteria. Heating it has the same effect so be careful there as well. If fermented foods are new to you, here are 8 Fast and Easy Probiotic Meals for Your Family full of flavor and health benefits.

**Organic Foods**

Organic foods are aligned with optimal gut health because they are free of pesticides, herbicides, antibiotics, and hormones all which can be disruptive to your gut flora balance and harmful to your overall health.

**Add a Probiotic Supplement to Your Diet for Extra Support**

If you are guilty of eating many of the “no” foods mentioned in this post as part of your everyday diet, gradually beginning to remove these foods for more healthy options is the first step to fostering a healthy microbiome and thus improving your overall health. In conjunction with taking a high-quality probiotic supplement, these changes will help to repopulate your healthy gut bacteria.

You also want to be sure the probiotic you choose as an effective delivery system. Standard capsules are not designed to withstand the harsh acidic environment of the stomach, meaning most of the most of the live organisms are killed off before they can reach your gastrointestinal tract (where your microbiome lives).

Our probiotic supplements are different! We use a patented time-release coating called BIO-tract®, scientifically proven to give our pills 15x more survivability than standard veggie capsules and powders. In other words, 15x as many of our CFUs make it past your stomach acid barrier and deep into your GI tract.

Probiotics also help to protect and nurture the health of your whole family right from the moment of birth. They support the pre and post-natal health of pregnant moms and the healthy development of infants and children.

The overall health benefits of adding a probiotic supplement to your daily diet are vast including increased metabolism (linked to weight loss), immune system support, increased nutrient absorption, better brain health, anti-inflammatory effects, and more.
References


Gut microbiome differs among ethnicities, researchers find

by Vanderbilt University

Graphical representation of the gut microbiome. Credit: Bordenstein Lab

Research increasingly links the gut microbiome to a range of human maladies, including inflammatory bowel disease, diabetes and even cancer. Attempts to manipulate the gut with food rich in healthy bacteria, such as yogurt or kombucha, are in vogue, along with buying commercial probiotics that promise to improve users' chances against illness.

Changing the gut microbiome to beat illness really does hold great potential, said Vanderbilt University biologist Seth Bordenstein, but first scientists must answer what constitutes a healthy gut microbiome and in whom. By studying data on nearly 1,700 Americans of varying genders, ages, weights and ethnicities, they learned that gut microbiome differences among ethnicities are the most consistent factor.

That discovery holds promise in the burgeoning field of individualized medicine, because it is far easier to change a person's microbiome than their genes—the other major markers for disease. In addition, many chronic diseases disproportionately affect ethnic minorities, with underlying causes of that difference unexplained. Perhaps some answers lie in the gut microbiome.
"Human genomes are 99.9 percent the same between any two people, so what we're really interested in is what explains the marked variations in gut microbiomes between people," said Bordenstein, associate professor of biological sciences. "What are the rules, and can we manipulate that microbiome in order to improve health and medicine in the long run? If you look at common factors associated with gut microbiome differences, such as gender, weight or age, you find many inconsistencies in the types of gut bacteria present. But when we compare differences by patients' self-declared ethnicities, we find stable and consistent features of bacteria present in the gut."

This chart demonstrates the differences in abundance of gut microbiota among varying ethnicities. Credit: Bordenstein Lab

The work was done in collaboration with a team at the University of Minnesota, and the results, outlined in a paper titled "Gut Microbiota Diversity across Ethnicities in the United States," appears today in the journal *PLOS Biology*.

The team discovered 12 particular types of bacteria that regularly vary in abundance by ethnicity. Because ethnicity captures many factors, ranging from diet to genetics, it's difficult to say why this is, said Andrew Brooks, the Vanderbilt doctoral student in the Vanderbilt Genetics Institute who analyzed data provided by the American Gut Project and Human Microbiome Project. But it's a baseline for understanding healthy microbiome differences among individuals.
Bordenstein is director of the Vanderbilt Microbiome Initiative, a collaboration among five Vanderbilt schools and colleges to advance microbial discoveries and, ultimately, get them into the hands of doctors for precision and preventative medicine.

"You may buy probiotics over the counter at a drugstore, but those are unlikely to affect your microbiome in a substantial way," Bordenstein said. "They often are at too low a dose, and they may not even be viable bacteria. Moreover, one size may not fit all. But with more of this kind of research, we can hone in on the relevant differences and doses of bacteria that may reverse illness or prevent it from developing in the first place."

https://www.semanticscholar.org/paper/The-influence-of-ethnicity-and-geography-on-human-Gaulke-Sharpton/2ef8142ea159b90f644443ab117acd3a6cd6f87f
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