Student Guarantee Instruments

GEP Commission (Gender Equality Plan) of the Department	•It works on the promotion of gender equality in the Department through initiatives and events aimed at students and teachers • gep.bbcd@uniroma1.it
GENERACT project	•Social Secretariat for orientation to anti-violence and anti-discrimination services •progetto.generact@gmail.com •https://www.instagram.com/generact_/
Confidential Counselor	•Advice and assistance to victims of sexual harassment in Sapienza •consiglieradifiducia.sapienza@uniroma1.it
Safe Zone in the Department	• People trained to provide support to LGBTQ+ people and for the prevention of gender-based violence
Student Ombudsman of the Faculty of Mathematical, Physical and Natural Sciences	• available to the Student Observatory to assist it in the exercise of its functions and to receive any complaints, observations and proposals • garantesmfn@uniroma1.it

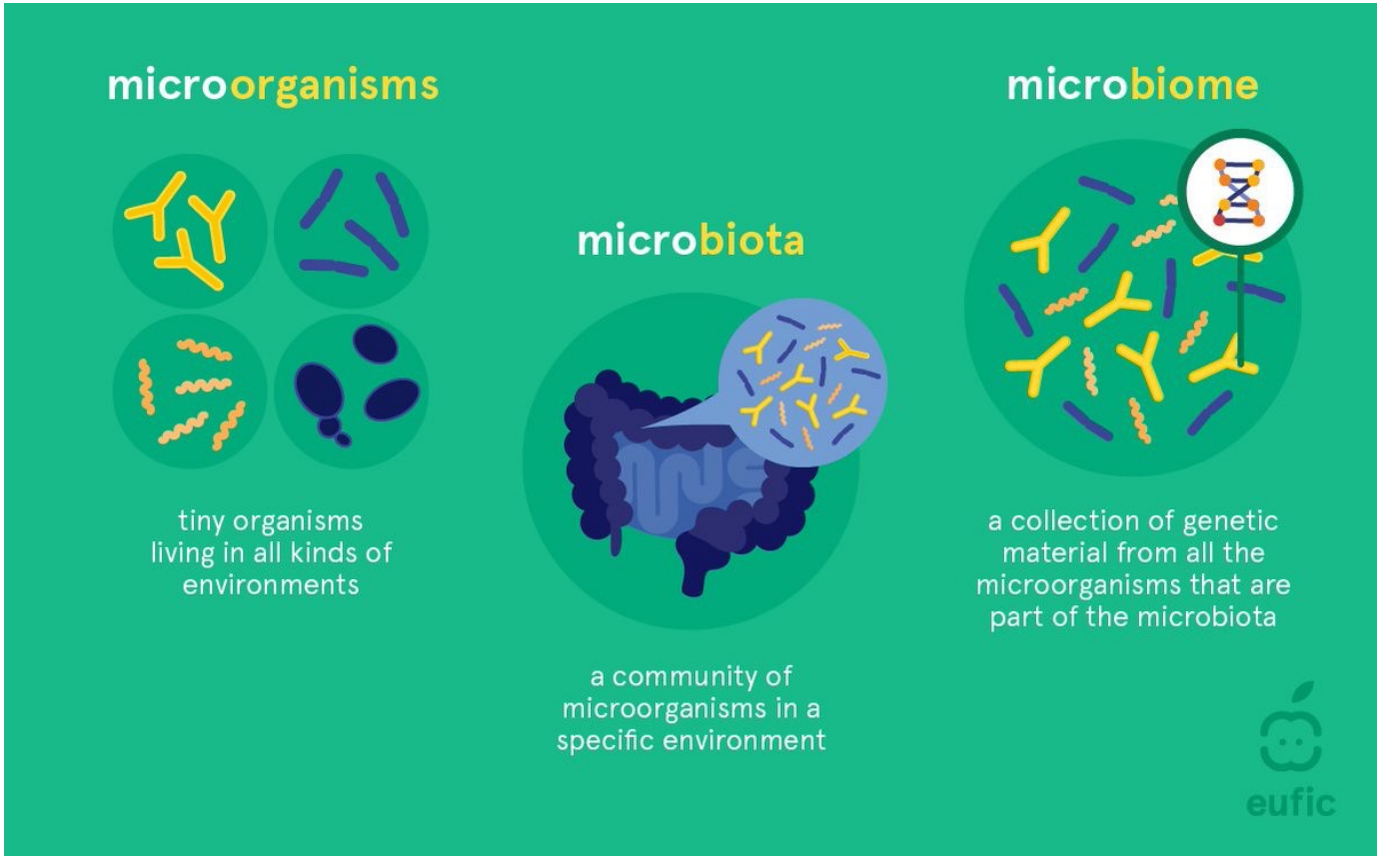
SAFE ZONE

Seen, heard or experienced something inappropriate in the Department?

Scan here – you can report it anonymously and safely.

The Microbiome

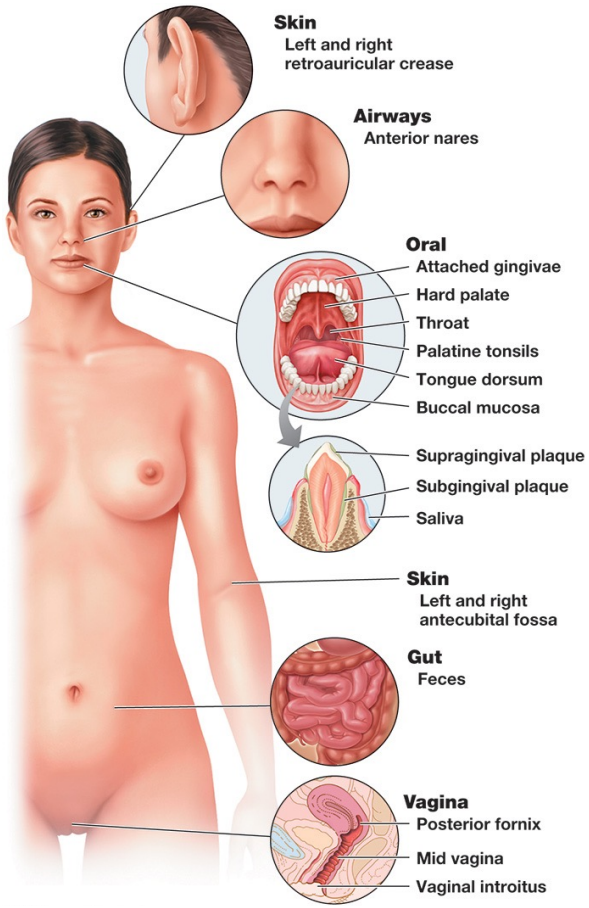
Defining the microbiome (or microbiota?)

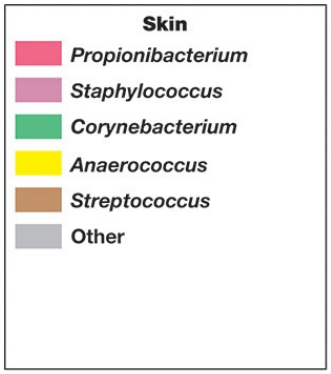


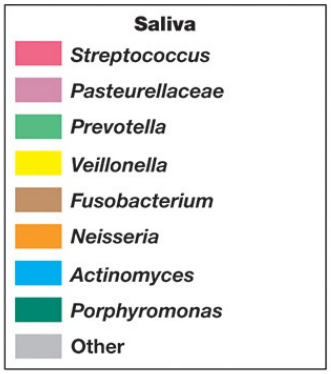
Microbiota in numbers

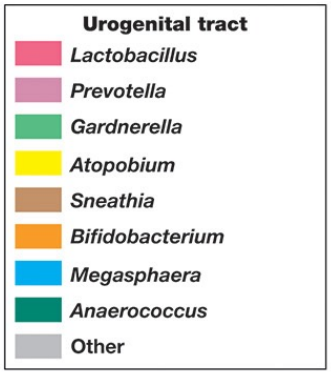
- For years it was believed that human body was harboring bacterial cells in a number that was 10x higher than the human cells
- However, a recent study reported that this ratio is more “1:1”: a 'reference man' (one who is 70 kilograms, 20–30 years old and 1.7 meters tall) contains on average about 30 trillion human cells and 39 trillion bacteria
- An estimated 500–1,000 species of bacteria exist in the human body at any one time, although the number of unique genotypes (subspecies) could be orders of magnitude greater than this.

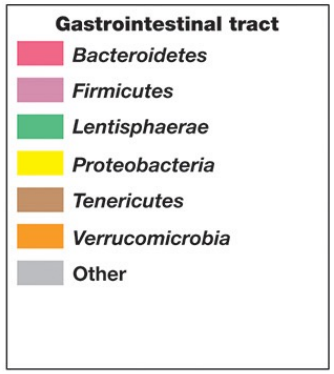
Microbiomes

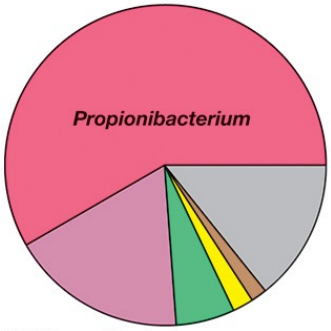


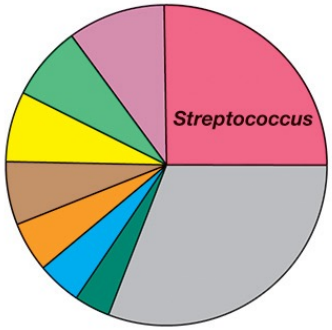


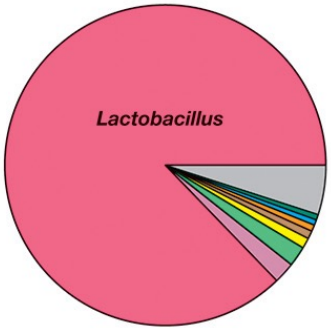


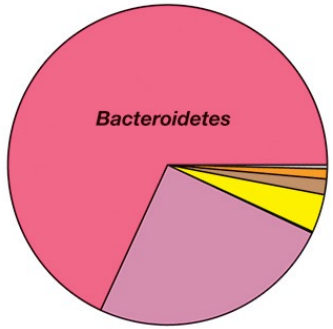






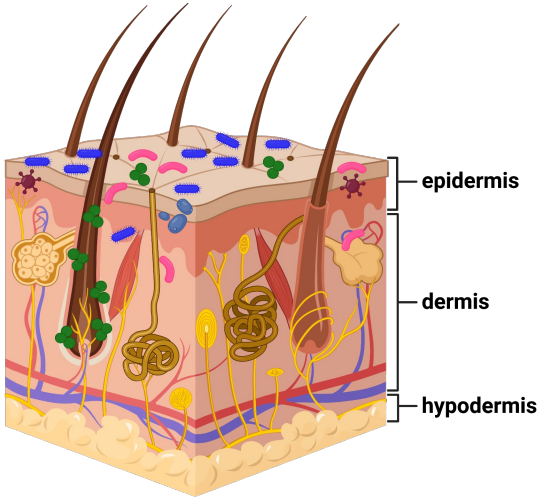


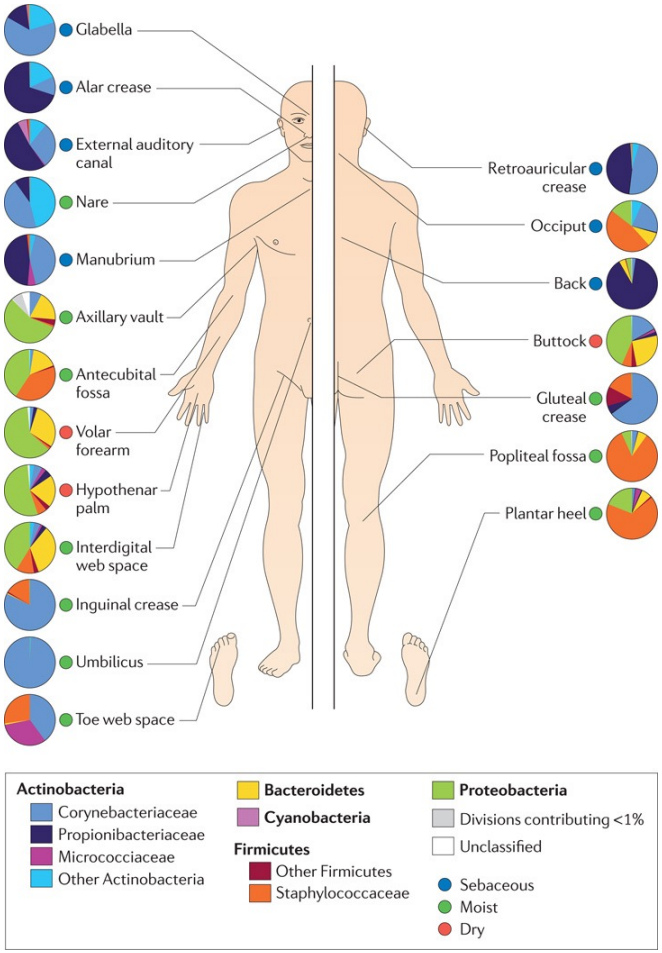




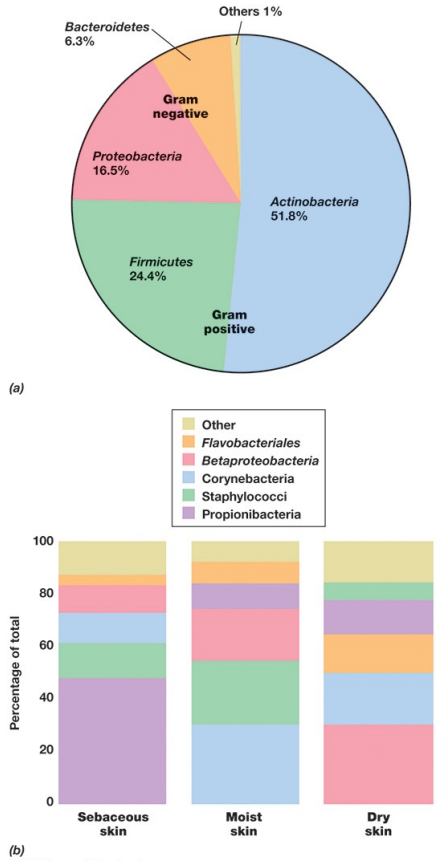
Different body parts have different microbiome

Skin is an ecosystem

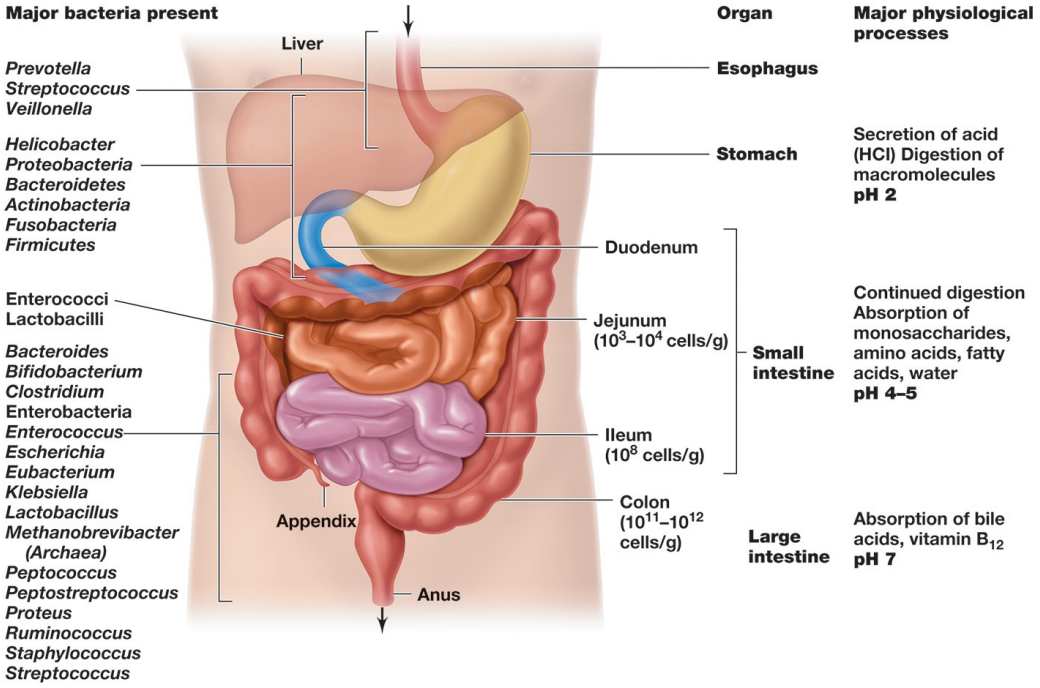




doi: 10.1111/j.1753-4887.2012.00493.x



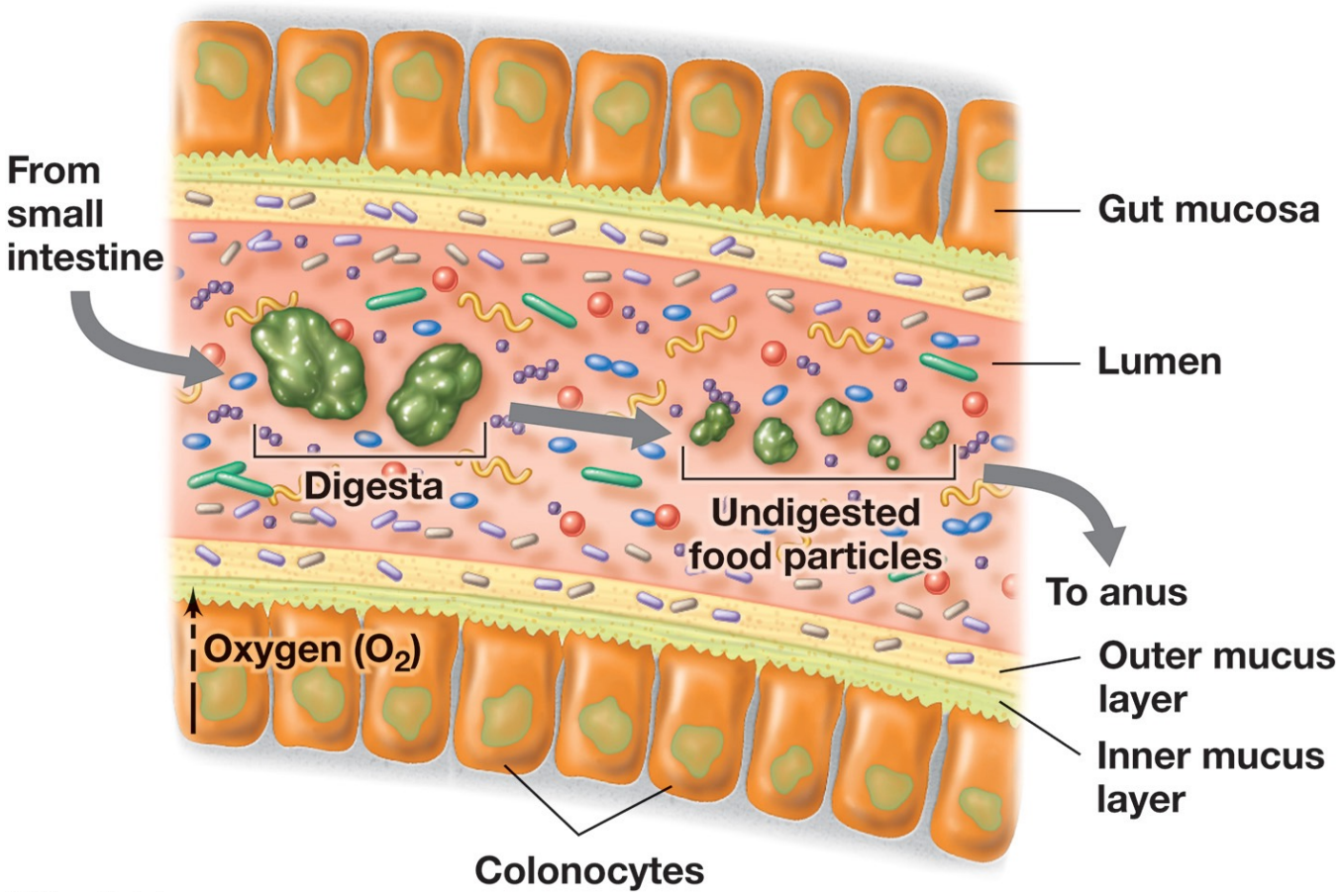
Different body parts have different microbiome



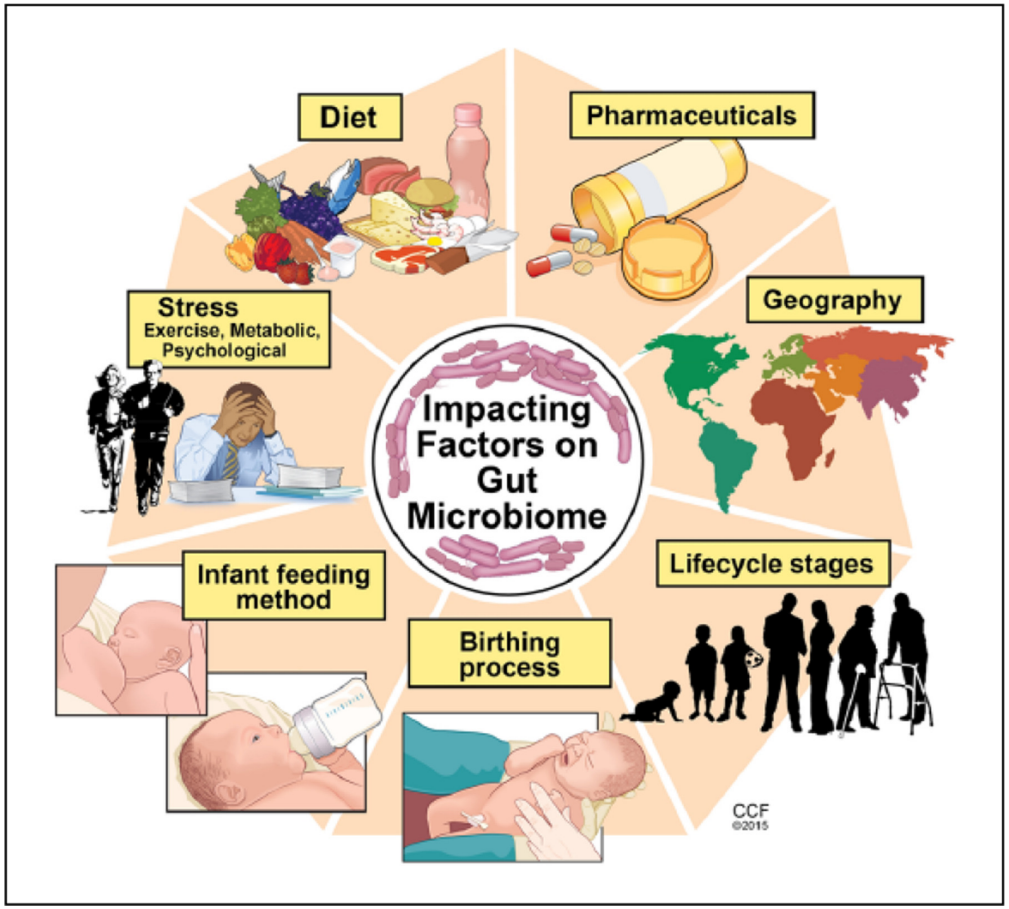
- This is true also for Gut microbiome.
- Studies report that GI microbiome is quite stable after the first 3 years after birth.
- Different parts of the GI have different conditions (digested food/pH/temperature/oxygen/IS cells).

doi: 10.1111/j.1753-4887.2012.00493.x

Spatial diversification of gut bacteria



Factors influencing the human microbiome



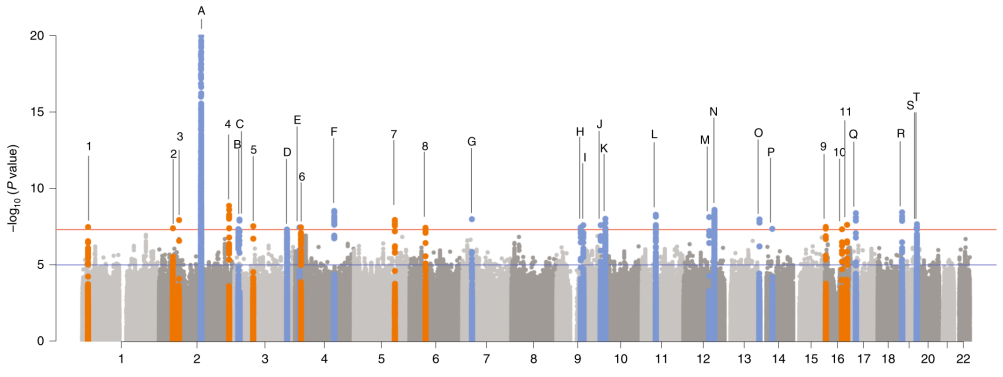
And also…

- Human genetics
- Body site
- Lifestyle/occupation
- Circadian rhythm

These factor interact: think of elderly people!
Changes in the microbiome structure of older individuals have often been attributed to altered lifestyles, diets, reduced mobility, decreased immune function, reduced intestinal capability, changed gut morphology, increased use of medication and drugs, and recurrent infections

Human genetic shapes the gut microbiome

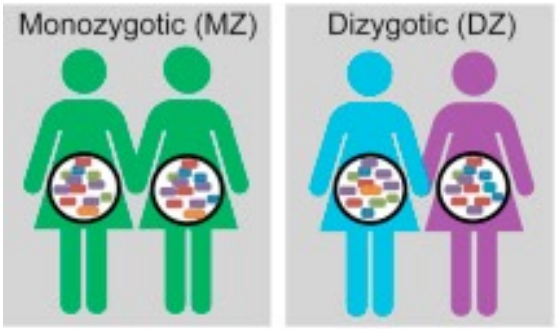
How can we determine this?
GWAS (Genome Wide Association Study) or Twin studies



Locus	*P* value	Type	Chr	rsID	Bacteria
A	1.28×10^{-20}	Quant	2	rs182549	Genus *Bifidobacterium*
B	4.66×10^{-8}	Quant	3	rs9864379	Order Gastranaerophilales
C	1.10×10^{-8}	Quant	3	rs75754569	Genus *Peptococcus*
D	4.88×10^{-8}	Quant	3	rs4428215	Family Oxalobacteraceae
E	3.55×10^{-8}	Quant	4	rs10805326	Genus *Intestinibacter*
F	3.06×10^{-9}	Quant	4	rs11098863	Genus *Enterorhabdus*
G	1.04×10^{-8}	Quant	7	rs17159861	Genus group *Eubacterium coprostanoligenes*
H	3.57×10^{-8}	Quant	9	rs602075	Genus *Allisonella*
I	2.57×10^{-8}	Quant	9	rs736744	Genus *Oxalobacter*
J	2.55×10^{-8}	Quant	10	rs12781711	Genus *Ruminococcaceae* UCG013
K	9.80×10^{-9}	Quant	10	rs61841503	Family Peptostreptococcaceae
L	5.29×10^{-9}	Quant	11	rs10769159	Genus *Ruminococcus1*
M	7.57×10^{-9}	Quant	12	rs12320842	Genus *Faecalibacterium*
N	2.58×10^{-9}	Quant	12	rs11110281	Genus *Streptococcus*
O	1.08×10^{-8}	Quant	13	rs7322849	Genus *Bifidobacterium*
P	4.42×10^{-8}	Quant	14	rs8009993	Genus *Ruminococcaceae* UCG009
Q	4.31×10^{-9}	Quant	17	rs7221249	Genus *Erysipelatoclostridium*
R	3.74×10^{-9}	Quant	19	rs67476743	Genus *Tyzzerella3*
S	4.26×10^{-8}	Quant	19	rs830151	Genus *Candidatus Soleaferrea*
T	2.21×10^{-8}	Quant	19	rs35866622	Genus group *Ruminococcus torques*
1	3.34×10^{-8}	Binary	1	rs555115	Genus *Turicibacter*
2	4.07×10^{-8}	Binary	2	rs57440956	Genus *Ruminiclostridium6*
3	1.17×10^{-8}	Binary	2	rs56081657	Genus *Odoribacter*
4	1.42×10^{-9}	Binary	2	rs7574352	Family Peptococcaceae
5	2.98×10^{-8}	Binary	3	rs17066404	Family Peptococcaceae
6	3.53×10^{-8}	Binary	4	rs207281	Genus *Enterorhabdus*
7	1.16×10^{-8}	Binary	5	rs62373497	Genus *Coprococcus1*
8	3.79×10^{-8}	Binary	6	rs9474033	Family Pseudomonadaceae
9	3.34×10^{-8}	Binary	16	rs437867	Genus *Lachnospiraceae* UCG010
10	4.67×10^{-8}	Binary	16	rs17319026	Genus *Anaerostipes*
11	2.42×10^{-8}	Binary	16	rs11647069	Family Bacteroidales S24.7

https://doi.org/10.1038/s41588-020-00763-1

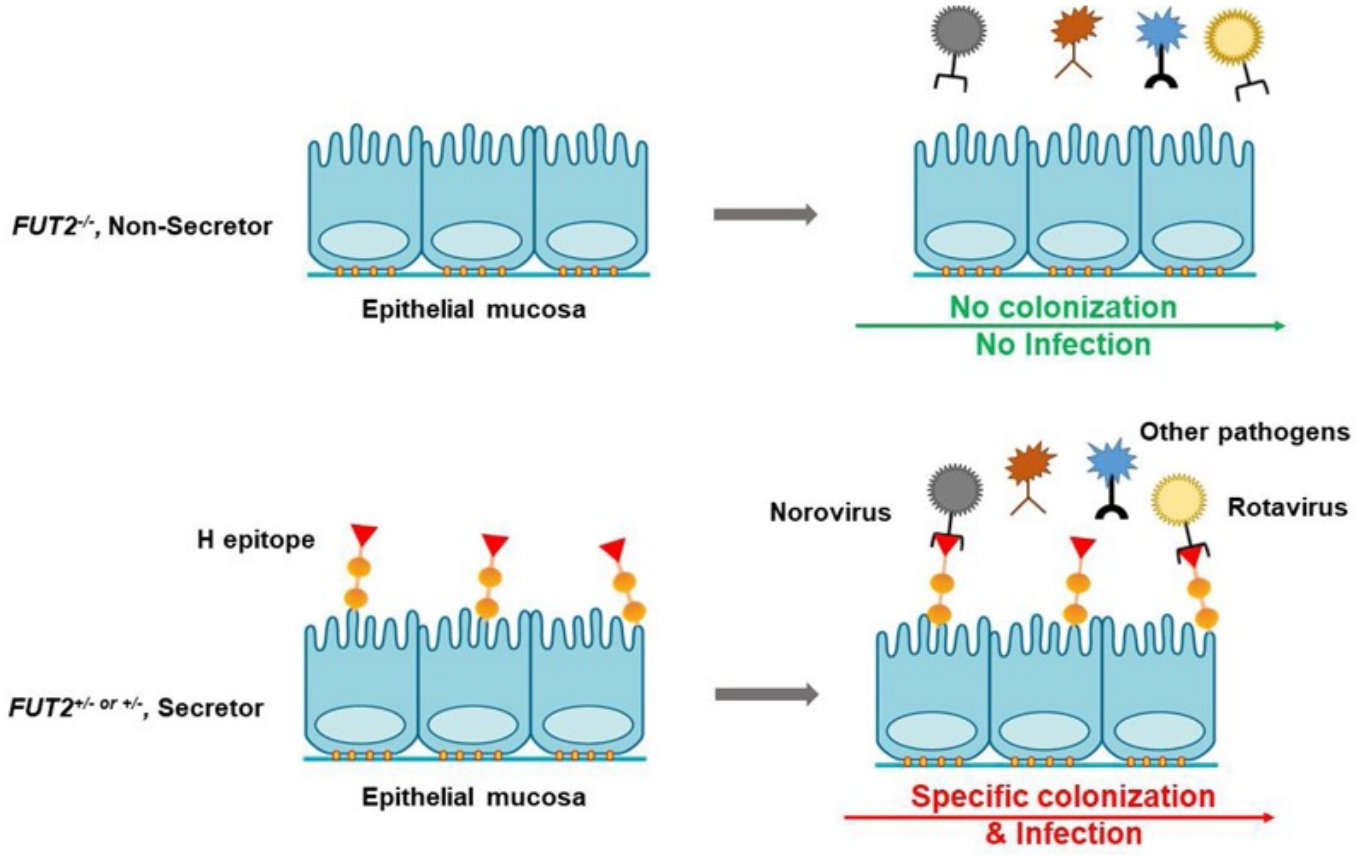
twinsUK



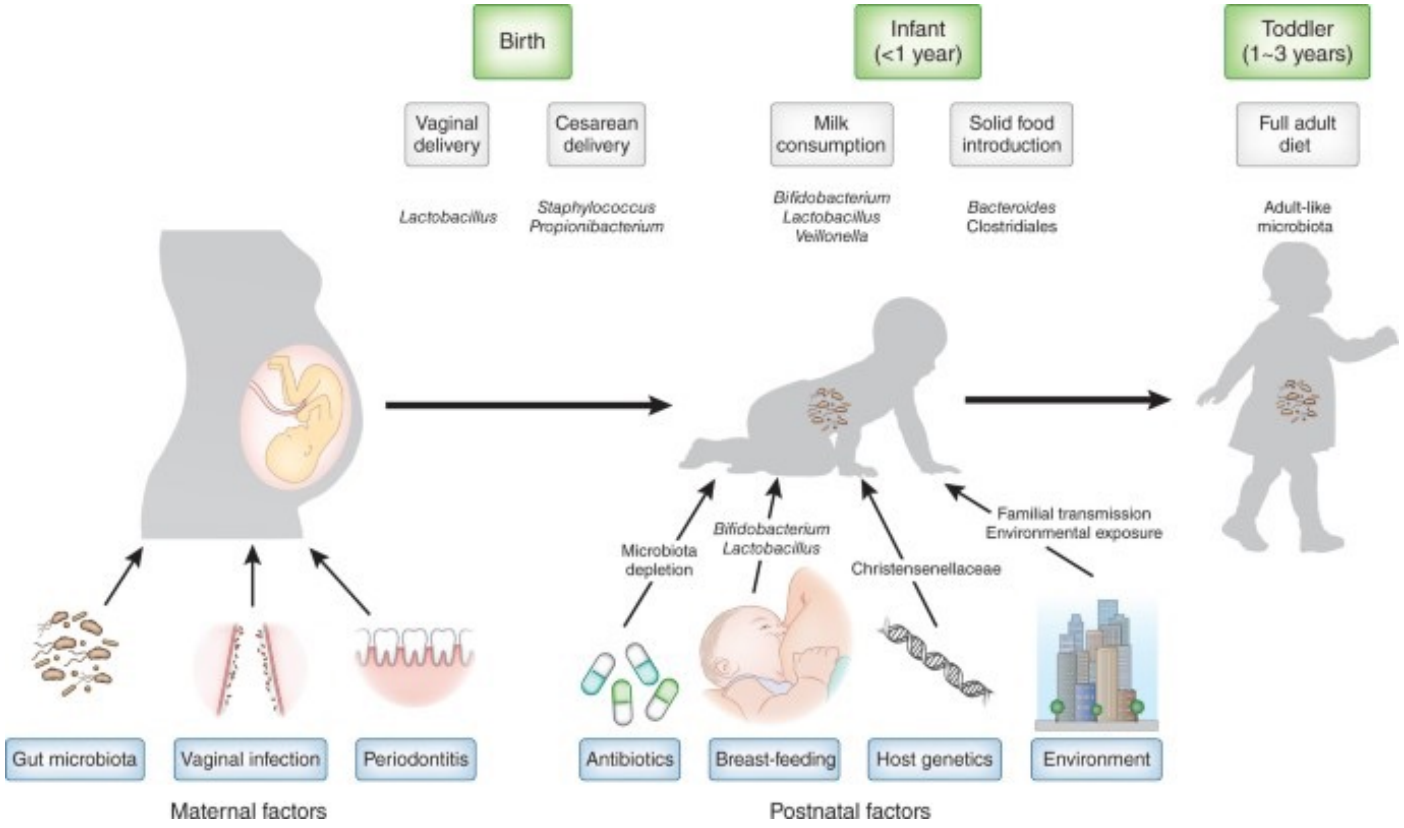
MZ twins have a more similar microbiota than DZ twins

https://doi.org/10.1016/j.cell.2014.09.053

Human genetic shapes the gut microbiome

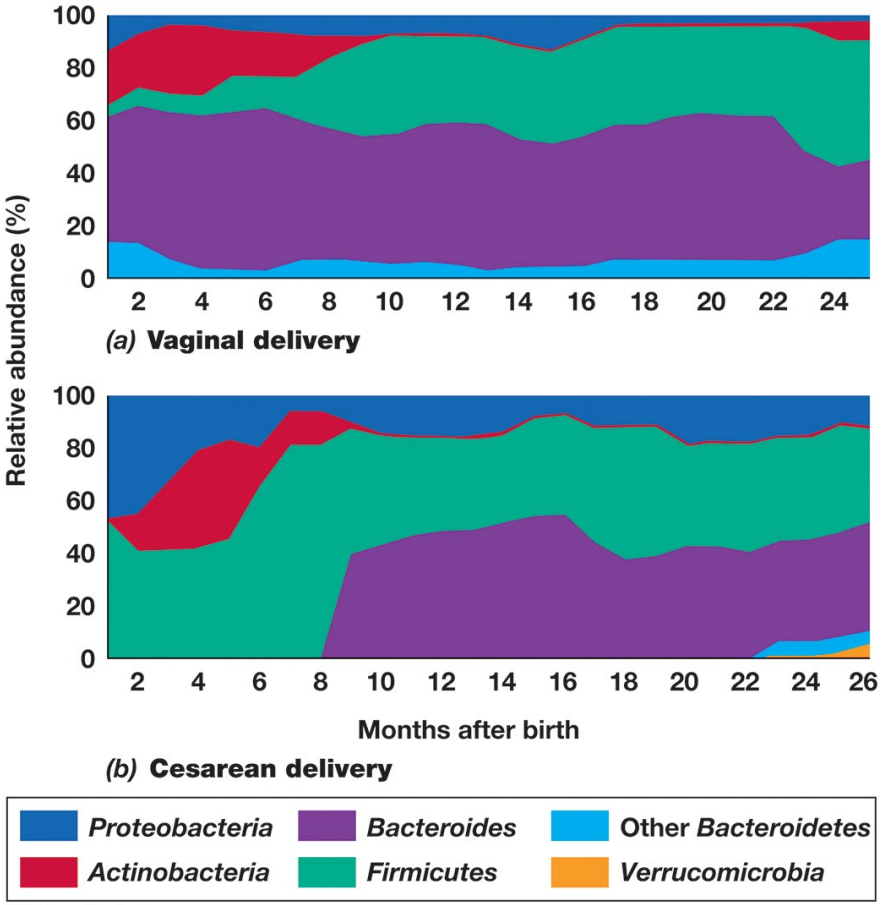


Microbiome colonization and development

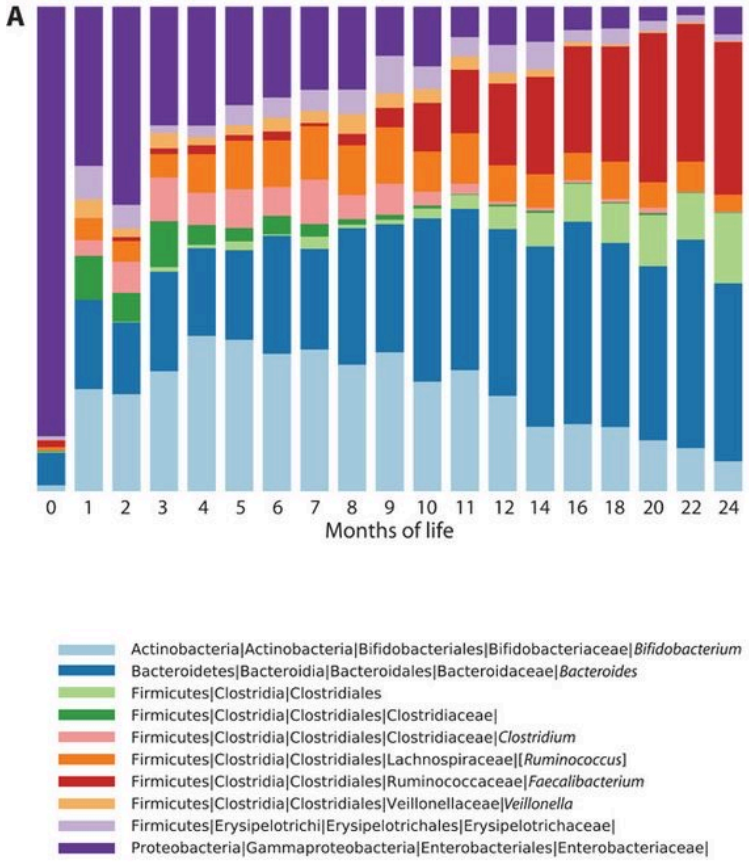


https://doi.org/10.1038/nm.4142

Impact of Birth Mode on the Young Infant's Gut Community



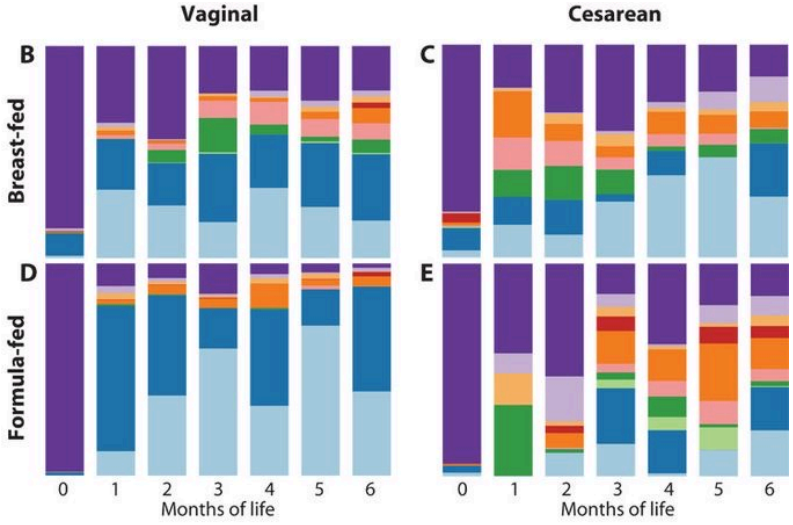
Microbiome colonization and development



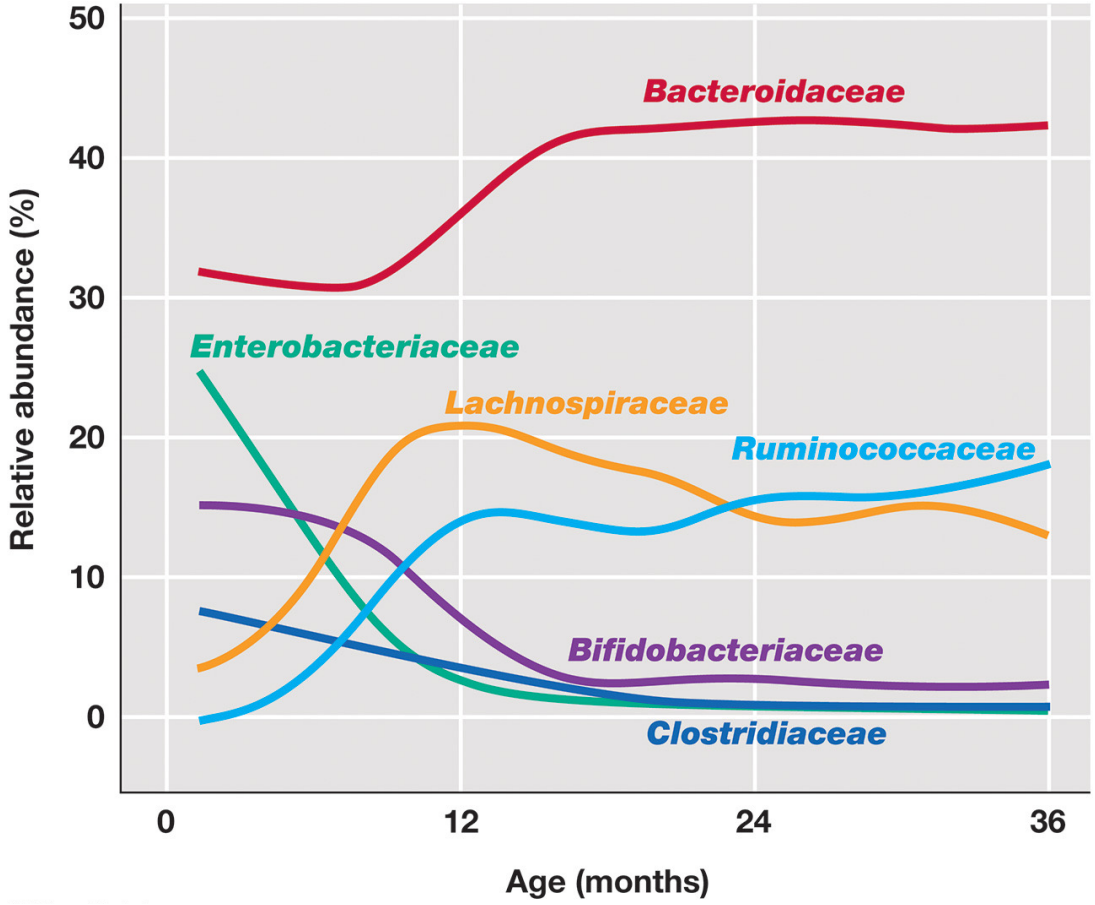
DOI: 10.1126/scitranslmed.aad7121

Microbiome composition is affected by:

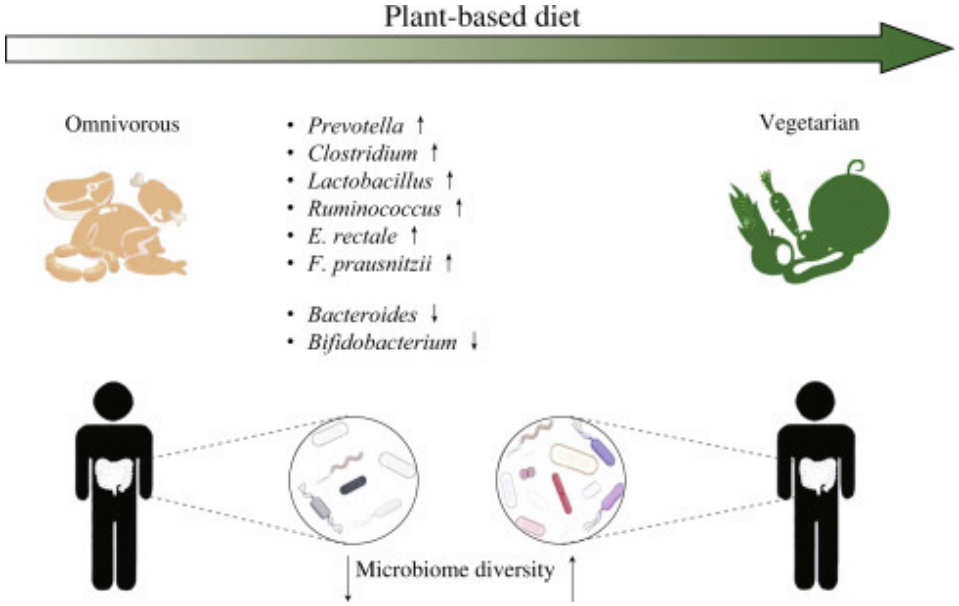
- Method of delivery
- Feeding method



Maturation of the Infant Gut Community



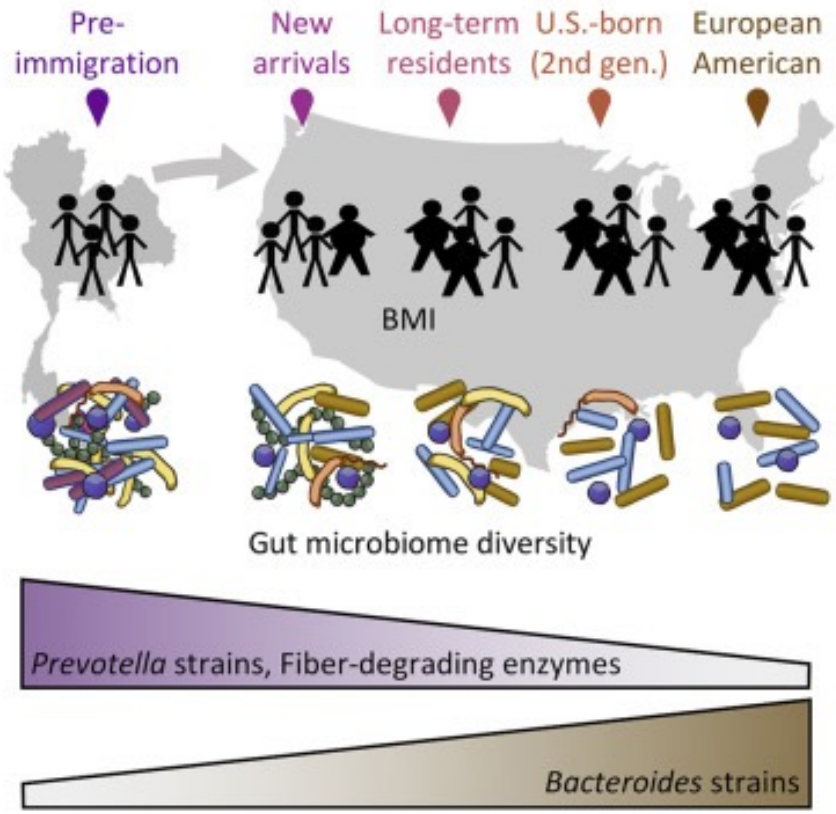
Diet influences the microbiome



https://doi.org/10.1016/j.fshw.2021.11.002

- plant-based diet promotes the development of more diverse and stable microbial systems.
- vegans and vegetarians have a distinctive microbiome.
- Polyphenols, also abundant in plant foods, increase *Faecalibacterium* and *Lactobacillus*, which provide anti-pathogenic and anti-inflammatory effects and cardiovascular protection.
- High fiber intake also encourages the growth of species that ferment fiber into metabolites as short-chain fatty acids (SCFAs with positive health effects, such as improved immunity against pathogens, blood–brain barrier integrity, provision of energy substrates, and regulation of critical functions of the intestine).

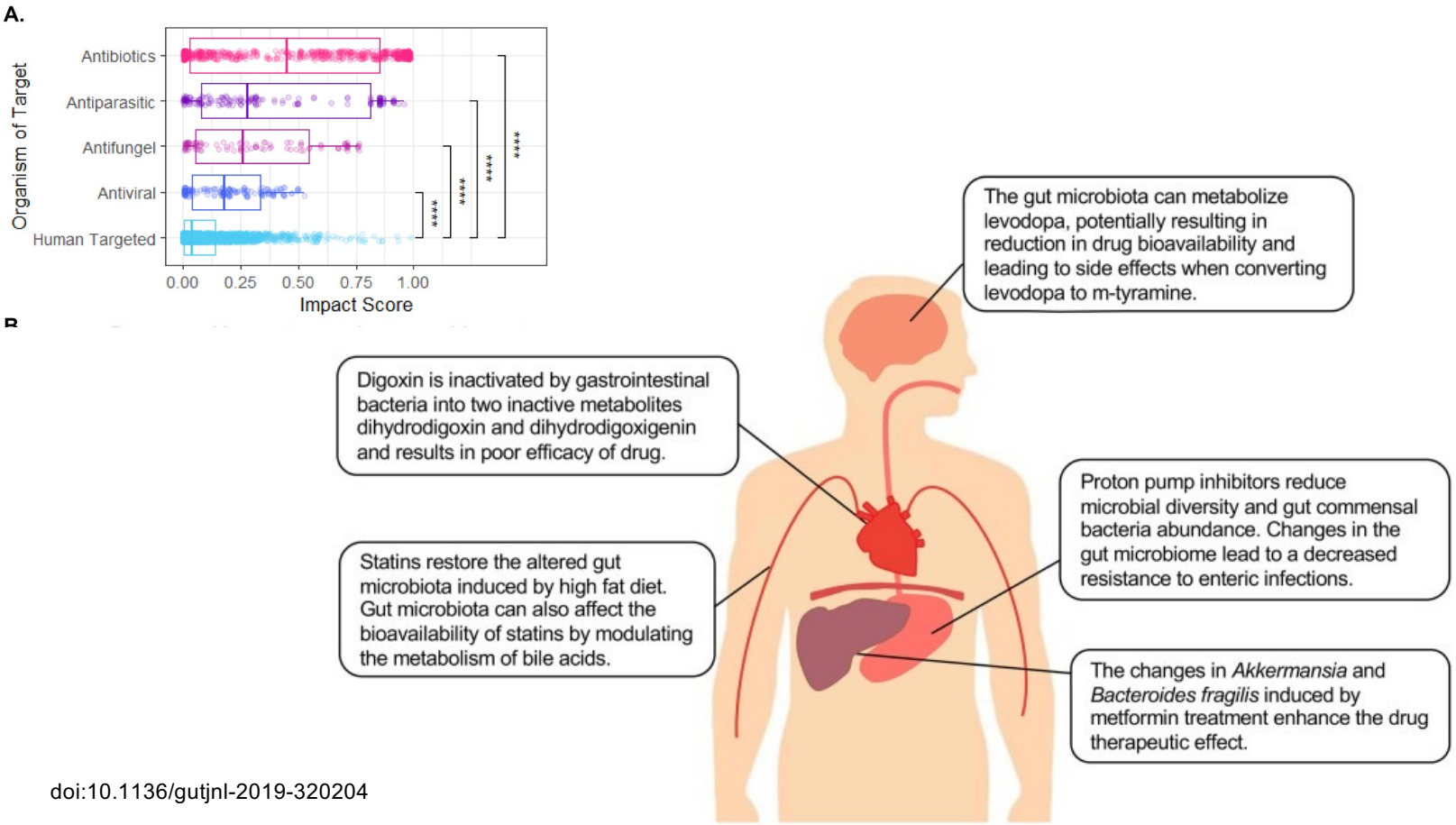
Diet influences the microbiome



- changing the diet of immigrants from Asia to the United States is linked to an immediate and intense change in the microbiome structure with an impact on their health and development of obesity and its associated diseases
- n=514

Fermented food are associated with beneficial increased diversity and reduced inflammation biomarkers.

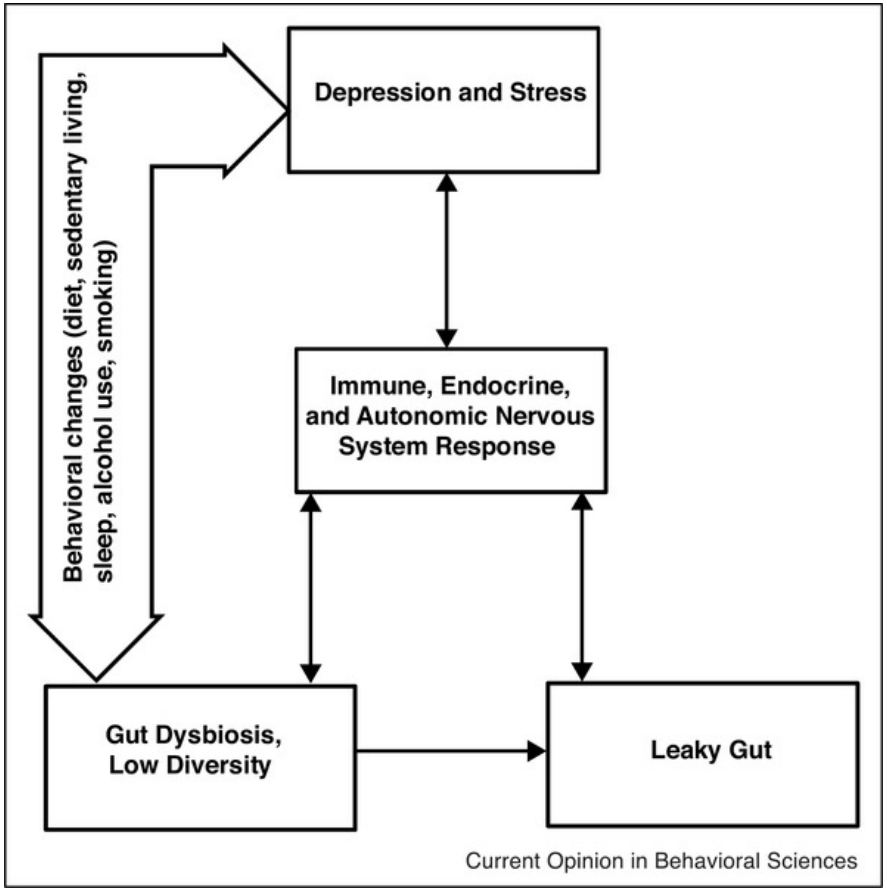
Drugs influence the microbiome and viceversa



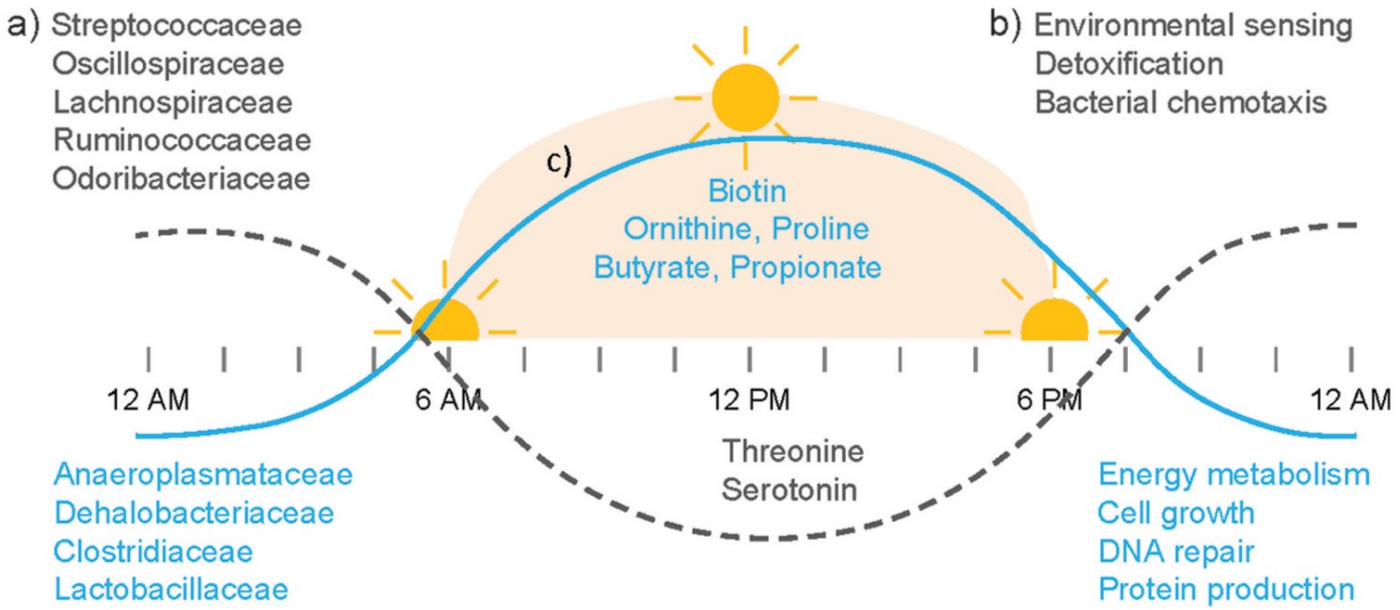
doi:10.1136/gutjnl-2019-320204

Stress affects the microbiome

- Several studies show that exposure to stress decreases the abundance of microbes with anti-inflammatory activity > which in turn decreases anti-inflammatory microbial metabolites such as SCFAs and contributes to a higher level of inflammation.
- The combination of stressful situations and infections or other inflammatory diseases worsen the outcome of the disease compared to non-stressed subjects.
- Consuming bacteria known for anti-inflammatory activity could be beneficial for people with anxiety disorder and high stress levels.

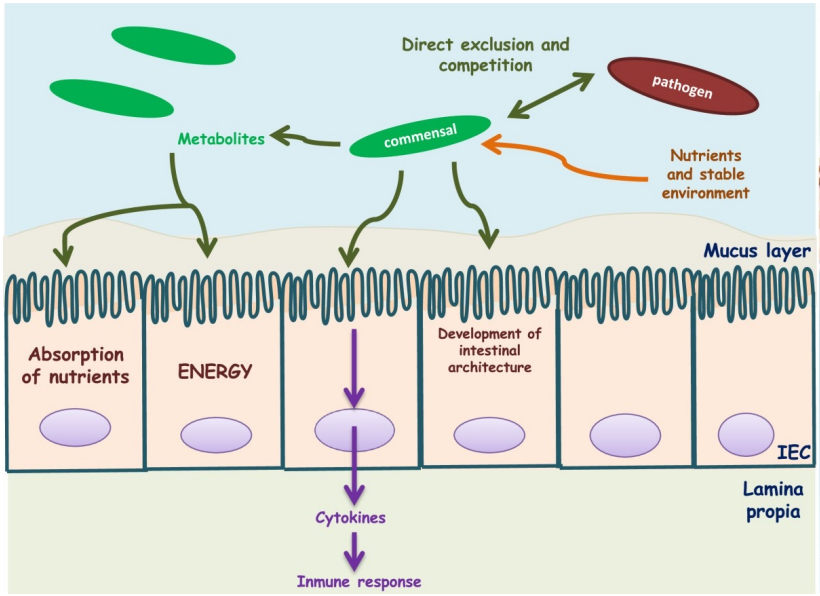


Circadian variation of microbiome

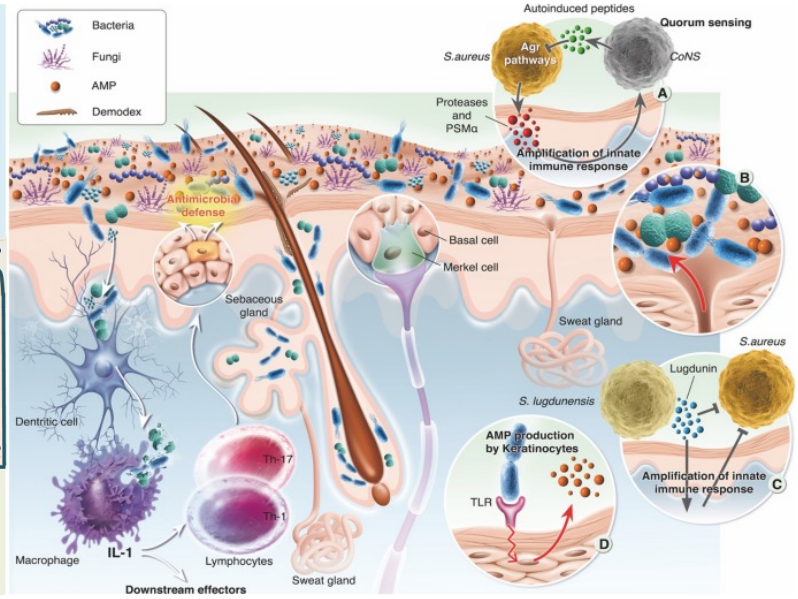


https://journals.sagepub.com/doi/10.1177/0748730417729066

A healthy microbiome has a beneficial role on the host



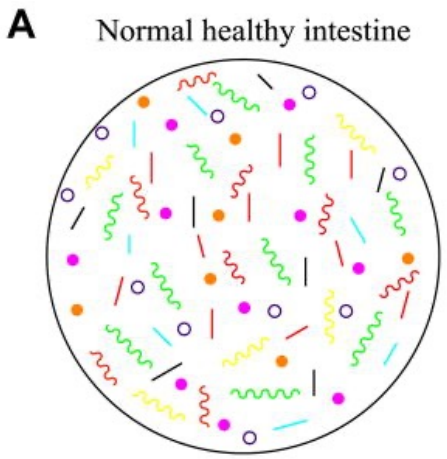
https://doi.org/10.1186/1475-2859-12-71

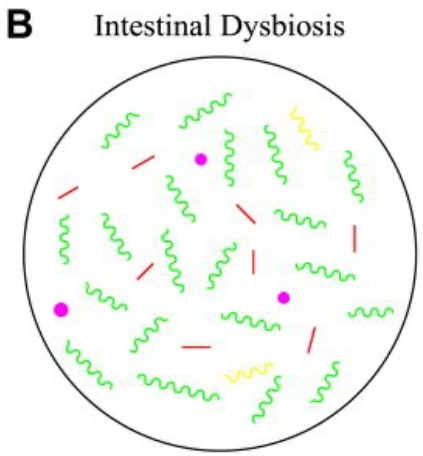


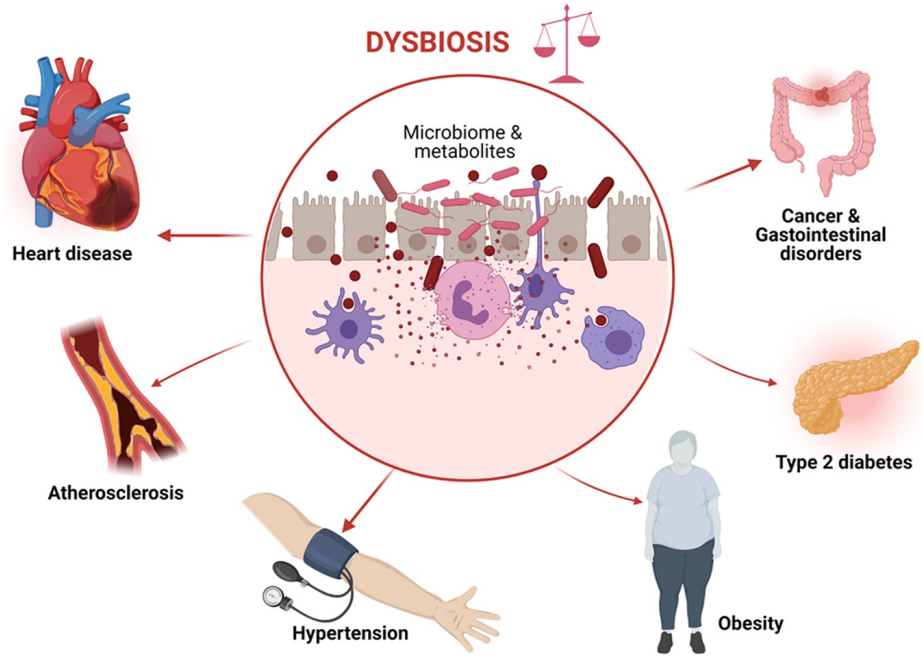
https://microbiomejournal.biomedcentral.com/articles/10.1186/s40168-021-01062-5

Process	Product or enzyme
Vitamin synthesis	Thiamine, riboflavin, pyridoxine, B_{12}, K
Amino acid synthesis[a]	Asparagine, glutamate, methionine, tryptophan, lysine, and others
Gas production	CO_2, CH_4, H_2
Odor production	H_2S, NH_3, amines, indole, skatole, butyric acid
Organic acid production	Acetic, propionic, butyric acids
Glycosidase reactions	***β***-Glucuronidase, ***β***-galactosidase, ***β***-glucosidase, ***α***-glucosidase, ***α***-galactosidase
Steroid metabolism (bile acids)	Esterified, dehydroxylated, oxidized, or reduced steroids

A shift from the healthy (balanced) microbiome composition is called dysbiosis: this could be either abnormal composition or reduced or enhanced biodiversity.







doi: 10.1097/MIB.0000000000000750
https://doi.org/10.1038/s41371-022-00698-6

Bioscience Reports (2021) **41** BSR20203850
https://doi.org/10.1042/BSR20203850

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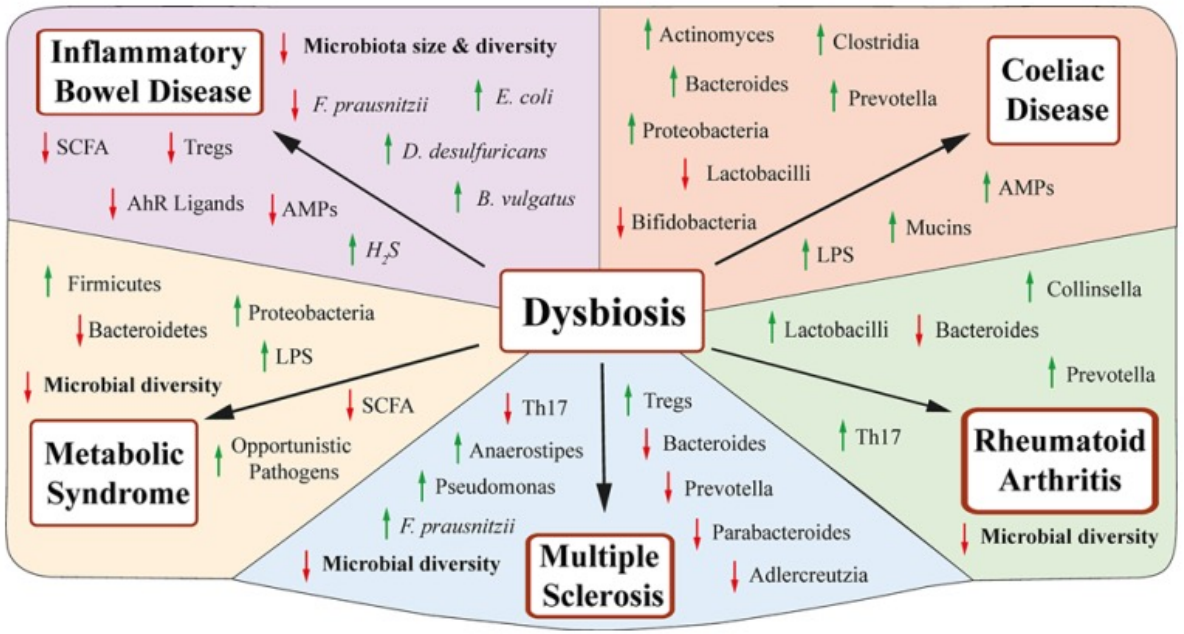
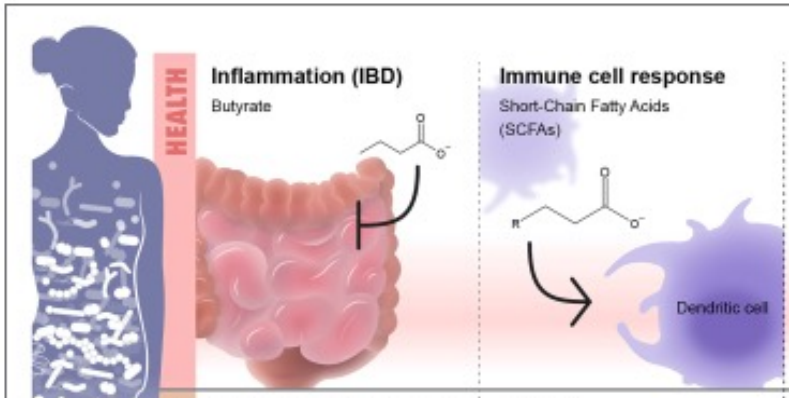


Body site	Main taxa in healthy individuals	Main alterations in disease	Associated diseases	References
Vagina	*Lactobacillus crispatus, L. iners, L. gasseri, L. jensenii Streptococcus, Bifidobacterium*	↑ *Sneathia, Atopobium, Gardnerella*	Bacterial vaginosis, Vulvovaginal infections (RVVI), HPV infections and cervical cancer	Felten et al. (1999), Zhou et al. (2007), Di Paola et al. (2017)
	Very low abundance of anaerobes, *Prevotella*, *Atopobium*, Sneathia Gardnerella	↓ Lactobacilli	Symptoms associated with these include discomfort, odor, discharge, infertility, and, if pregnant, could even lead to miscarriages	
Skin	*Staphylococcus, Propionibacterium, Corynebacterium*, and *Streptococcus*	↑ *S. aureus, S. epidermidis, P. acnes,* Proteobacteria	Psoriasis, atopic dermatitis, systemic lupus erythematosus and alopecia	Chang et al. (2018), Ho et al. (2019), Paller et al. (2019), Bay et al. (2020), Huang et al. (2020)
		↓ *Acinetobacter Cutibacterium, Propionibacterium, Corynebacterium*, and *Staphylococcus*		
Eye	*Staphylococcus, Propionibacterium*, and *Pseudomonas*	↑*Delftia* and *Bacteroides*	Keratoconjunctivitis, mucosa-associated lymphoid tissue (MALT) lymphoma, and high glucose levels on the ocular surface due to diabetes	Asao et al. (2019), Li et al. (2019), Suzuki et al. (2020)
		↓Proteobacteria and Acinetobacter		
Ear	*Corynebacterium*, *Staphylococcus*, and *Propionibacterium*	↑ *Haemophilus*, *Alloiococcus Staphylococcus, Turicella, Moraxella, Streptococcus* and *Stenotrophomonas*	Otitis media infections: Acute Otitis Media (AOM) or Chronic Otitis Media with Effusion (COME)	Lappan et al. (2018), Jervis-Bardy et al. (2019), Kolbe et al. (2019)
Nasopharyngeal tract	*Corynebacteriaceae, Staphylococcaceae, Peptoniphilaceae, Carnobacteriacea, Staphylococcus, Corynebacterium, Alloiococcus, Haemophilus, Streptococcus, Granulicatella*, and *Moraxella*	↑ *Streptococcus, Haemophilus, Moraxella,* Proteobacteria, *Escherichia, Roseateles,* and *Pseudomonas*	Asthma, influenza A virus (IAV), bronchiolitis, and rhinosinusitis acute respiratory illness (ARI)	Teo et al. (2015), Stewart et al. (2017), Copeland et al. (2018), Wen et al. (2018), Kang and Kang, (2021)
		↓*Corynebacterium, Moraxella* and *Dolosigranulum*		
Oral	*Streptococcus, Gemella, Abiotrophia, Granulicatella, Rothia, Neisseria*, and *Prevotella*	↑ *Porphyromonas, Tannerella, Prevotella, Filifactor*	Dental cavities, gingivitis, periodontitis, oral cancer	Dewhirst et al. (2010), Crielaard et al. (2011), Huang et al. (2011), Kennedy et al. (2019), Sulyanto et al. (2019)
Gastrointestinal tract	*Clostridium, Bacteroides, Lactobacillus, Coprobacillus, Escherichia/Shigella, Bifidobacterium, Faecalibacterium prausnitzii, Eubacterium rectale, Akkermansia muciniphila, Enterococcus, Streptococcus, Veillonella, Prevotella, Helicobacter pylori, Stenotrophomonas, Lactococcus, Bacillus, Solibacillus, Pseudomonas, Arthrobacter, Lysinibacillus*	↑ *Veillonella, Fusobacterium, Prevotella* and *Gemella, Parvimonas* and other Proteobacteria	Gastroesophageal reflux disease (GERD), Barrett's esophagus, or esophageal carcinoma, appendicitis	Pei et al. (2004), Maldonado-Contreras et al. (2011), Zoetendal et al. (2012), Guinane et al. (2013), Liu et al. (2013), Khan et al. (2014), Angelakis et al. (2015), Sundin et al. (2017), Gong et al. (2019), Fan et al. (2020), James et al. (2020)
		↓ *Bacteroides, Eubacterium rectale, Faecalibacterium prausnitzii, Akkermansia muciniphila* and Spirochaetes		

Dysbiosis: consequences of an unbalanced microbiota

1. Increased risk of infection
2. Gastrointestinal disorders
3. Chronic inflammation
4. Increased risk of obesity and metabolic diseases
5. Skin problems
6. Immune system dysfunction

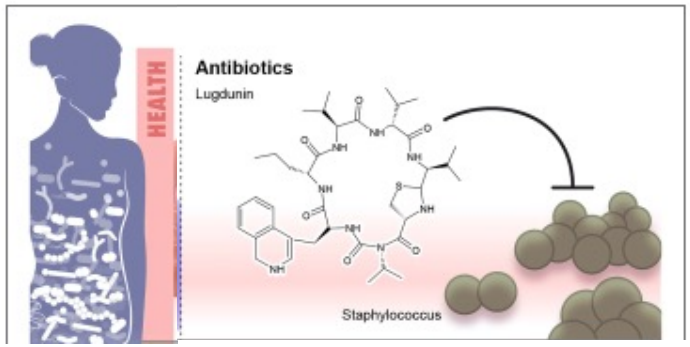
Beneficial effects of some members of the microbiota



Immune tolerance to self and harmless antigens and the fight against pathogens

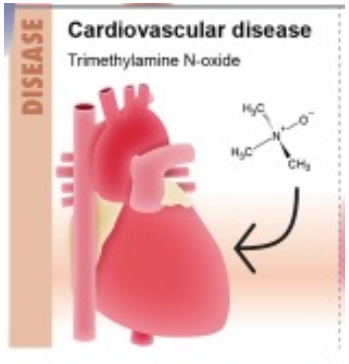
- Inflammatory bowel disease (IBD) is a general term that refers to a group of chronic disorders characterized by persistent inflammation of the gastrointestinal tract. The two main types of IBD are Crohn's disease and ulcerative colitis.
- Butyrate is a short-chain fatty acid produced by gut bacteria during the fermentation of dietary fiber.
- It has several beneficial effects, including reducing intestinal inflammation and supporting intestinal mucosal health.
- Several studies have shown that IBD patients have lower levels of butyrate-producing bacteria.
- Some studies have shown that the administration of butyrate can improve the disease.

Beneficial effects of certain members of the microbiota (a single one...)



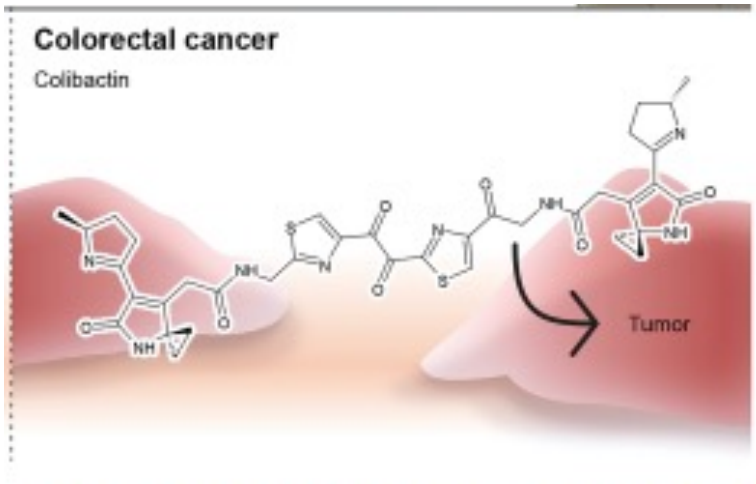
- Lugdunine is a natural antibiotic produced by a strain of commensal bacteria called *Staphylococcus lugdunensis*
- Lugdunine has been identified as a potent antibacterial agent against a wide range of pathogenic bacteria, including certain strains of *Staphylococcus aureus*, a pathogen known for its resistance to antibiotics.
- Effective against pathogenic strains of bacteria without causing significant damage to the commensal microbiota.

Negative effects of some members of the microbiota (individual...)



- Trimethylamine-N oxide (TMAO) is the major diet-induced metabolite produced by the gut microbiota and is eliminated primarily through renal excretion.
- TMAO has been correlated with an increased risk of atherosclerotic cardiovascular disease and related complications, such as cardiovascular mortality or major adverse cardiovascular events.
- TMAO precursors are present in the human diet and are metabolized into TMAO by the gut microbiota and various enzymes.
- Diet plays a key role in generating TMAO. L-carnitine and choline are mainly present in foods of animal origin.
- In addition, the gut microbiota has been shown to be essential for converting dietary compounds into TMA, and changes in the gut microbiota have marked effects on TMAO levels.

Negative effects of some members of the microbiota (single and cumulative)



- Gut dysbiosis has also been linked to colorectal cancer (CRC)
- In patients with CRC, a general dysbiosis has been found which involves a decrease in butyrate-producing bacteria together with an increase in the proportion of several potentially pathogenic bacteria.
- The bacterial genotoxin colibactin promotes colon cancer growth by modifying the tumor microenvironment.