MICROBIOLOGIA GENERALE

Microbial interactions with animals: the microbiome

Relationships of microorganisms with animals: the symbioses

Interaction	Species A	Species B
Commensalism	Receives benefit	Not affected
Mutualism	Receives benefit	Receives benefit
Parasitism	Receives benefit	Harmed

Mutualism (+ +)

Commensalism (0 +)

Pathogens (- +)

Obliged: always cause of disease.

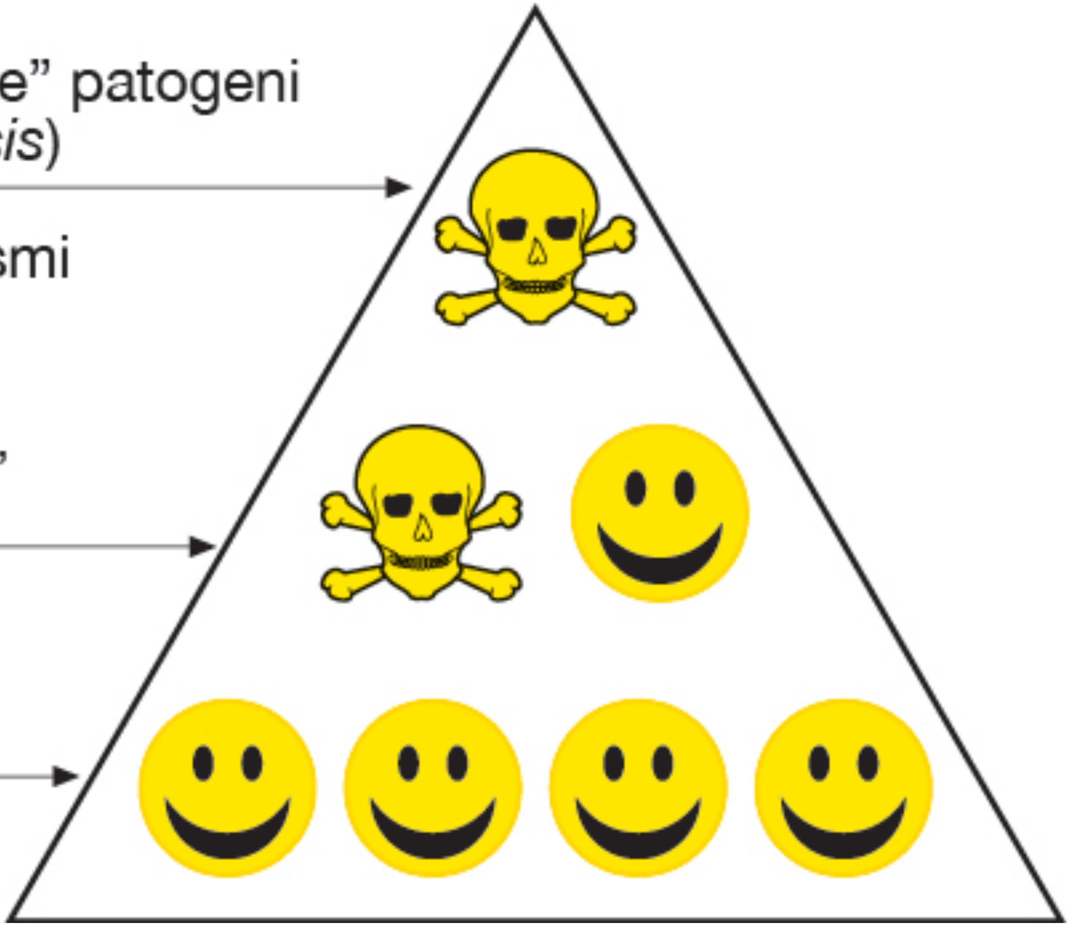
Mycobacterium tubercolosis

Neisseria gonorrhoeae

Opportunistics: belong to the normal microbiota

Staphylococcus aureus

Escherichia coli

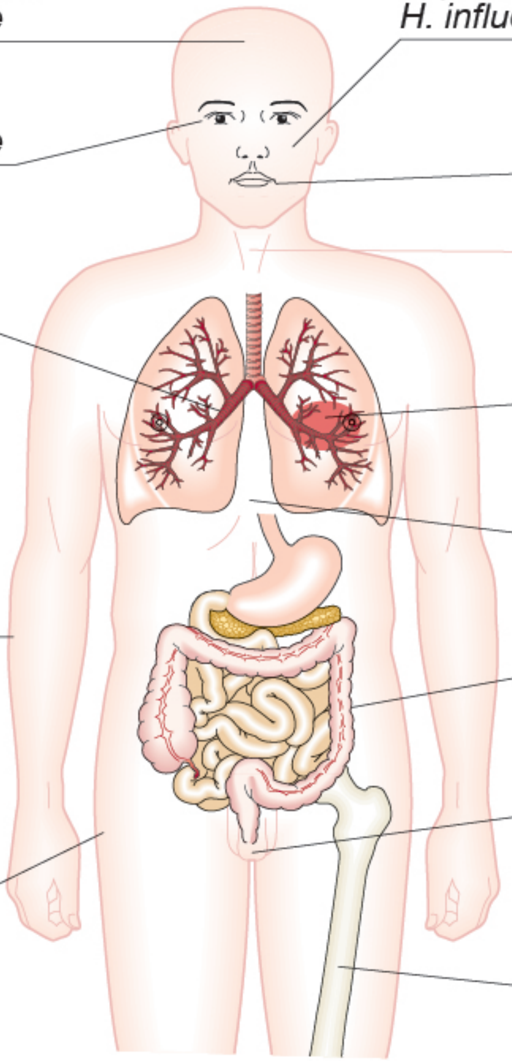


Solo pochi batteri sono “sempre” patogeni
(es. *Mycobacterium tuberculosis*)

Un certo numero di microrganismi
sono patogeni solo in
determinate circostanze
(es. *Streptococcus epidermidis*,
Escherichia coli)

Molti microrganismi possono
instaurare relazioni benefiche
con l’ospite

Human opportunistic bacterial pathogens



Meningite
S. pneumoniae
N. meningiditis
H. influenzae

Infezioni oculari
S. aureus
H. influenzae

Polmonite
S. pneumoniae
H. influenzae

Infezioni cutanee
S. pyogenes
S. aureus
P. acnes

(Gangrena) *C. perfringens*

S. pneumoniae
H. influenzae
Otite media

S. mutans **(Carie)**
Porphyromonas gingivalis **(Paradontite)**

Strep. pyogenes **(Faringite)**

S. sanguis
(Endocardite batterica)

H. pylori
(Gastrite, tumore)

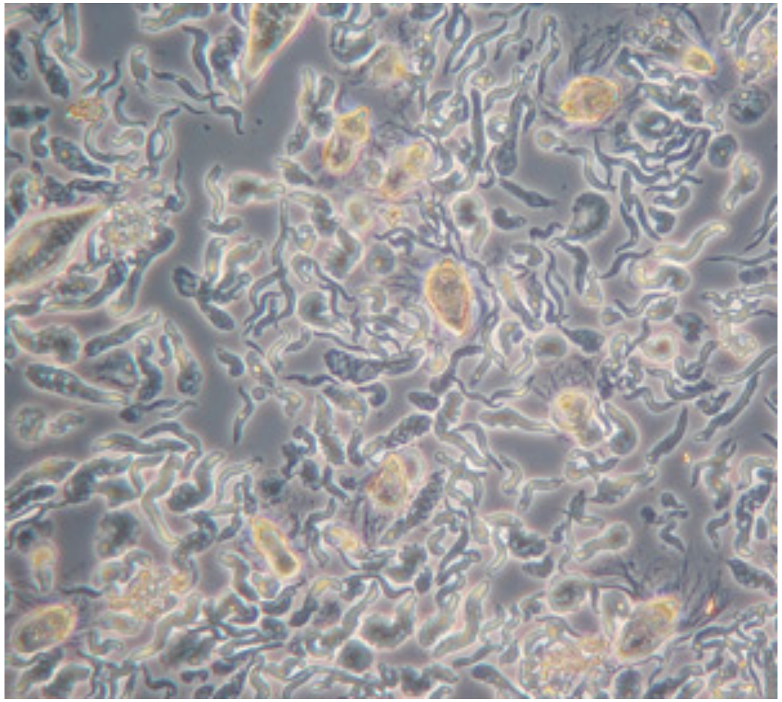
C. difficile
(Enterocolite pseudomembranosa)

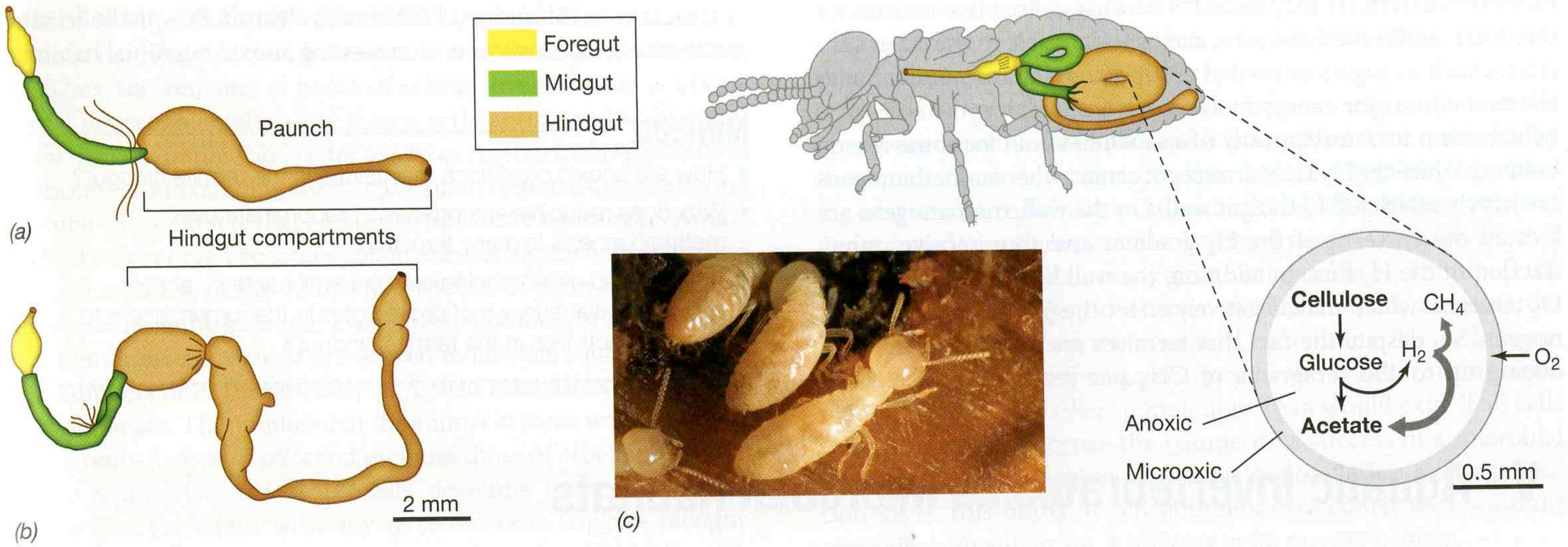
E. coli
(Infezione apparato urinario)

S. aureus **(Osteomielite)**

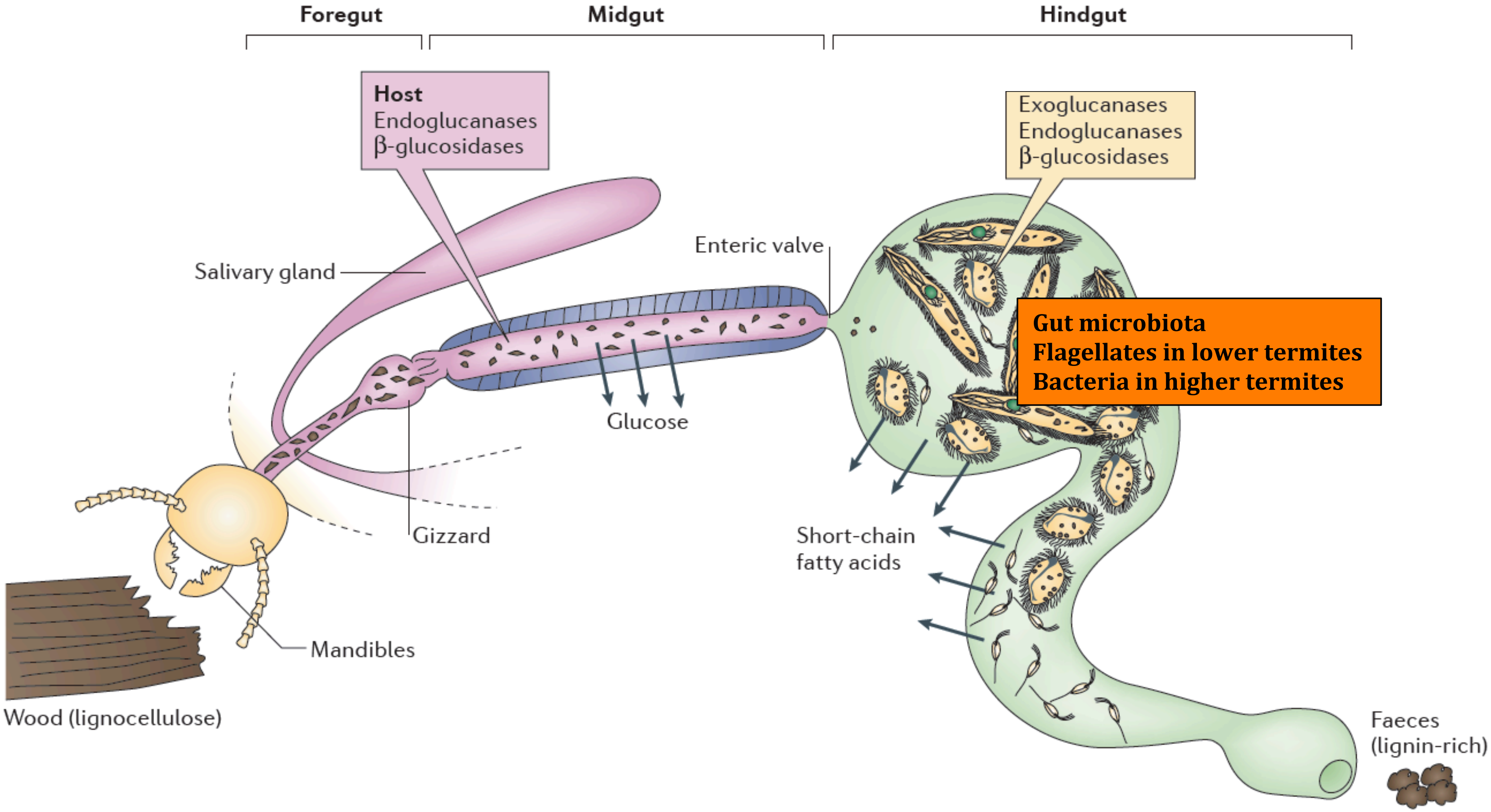
Insects as Microbial Habitats

Termites



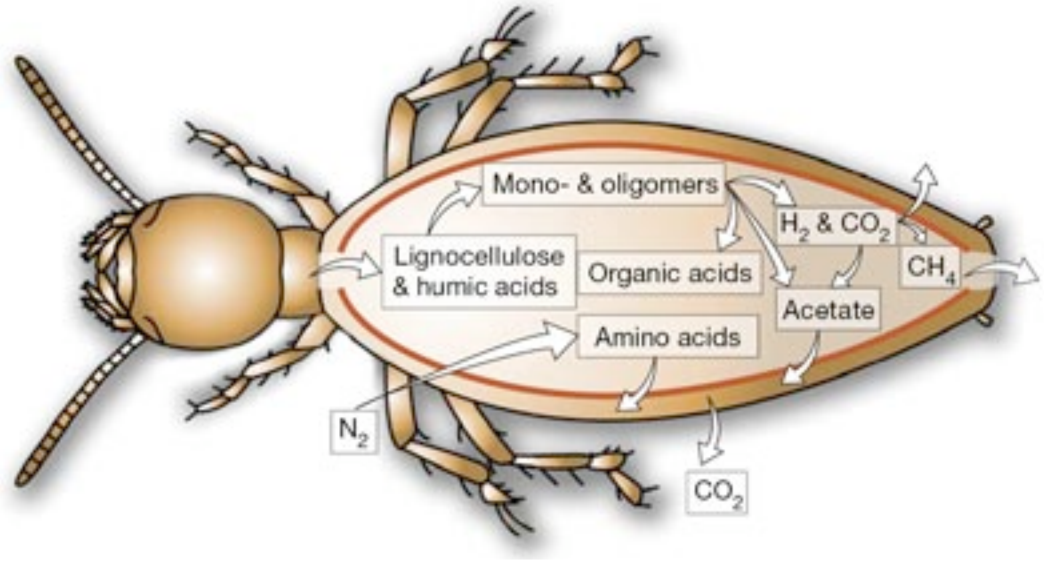

🟨 Foregut
🟩 Midgut
🟫 Hindgut
Paunch
Hindgut compartments
(a)
(b)
2 mm
(c)
Cellulose
Glucose
H_2
CH_4
O_2
Acetate
Anoxic
Microoxic
0.5 mm

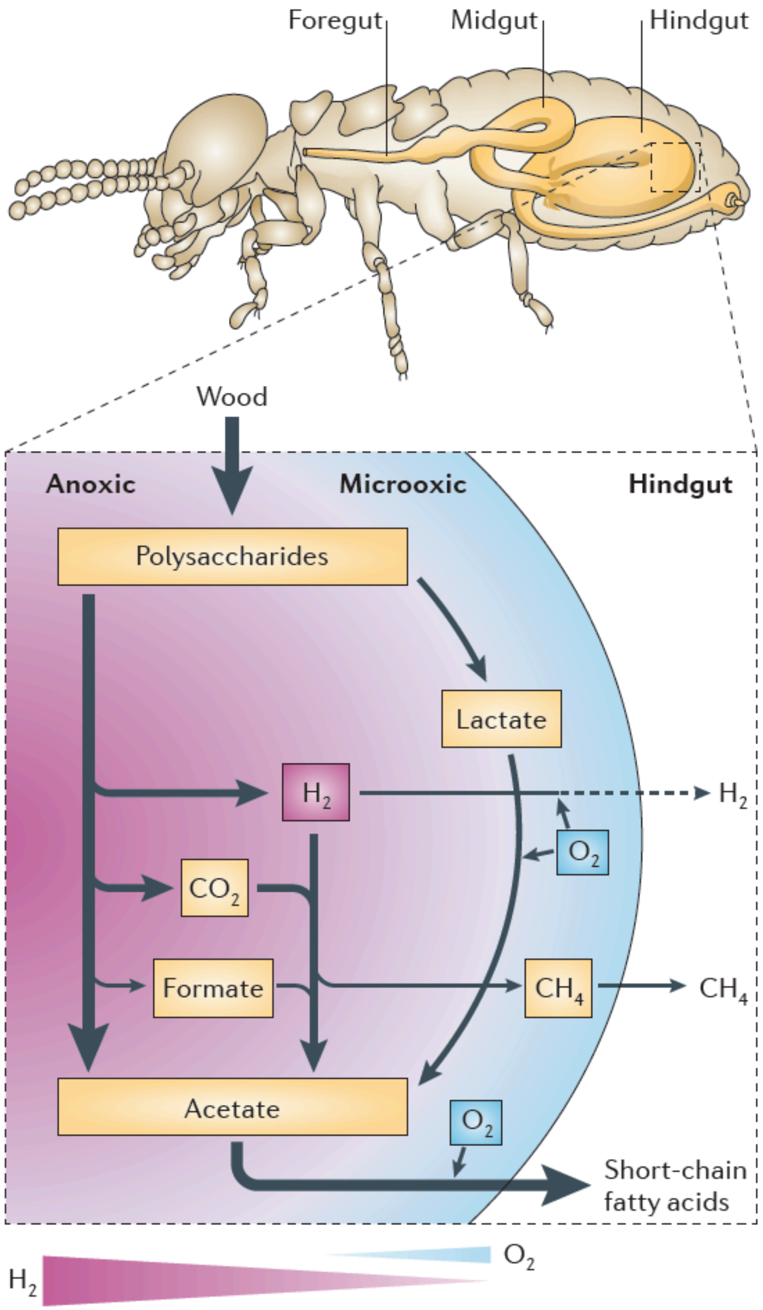
The cellulolytic systems of termites



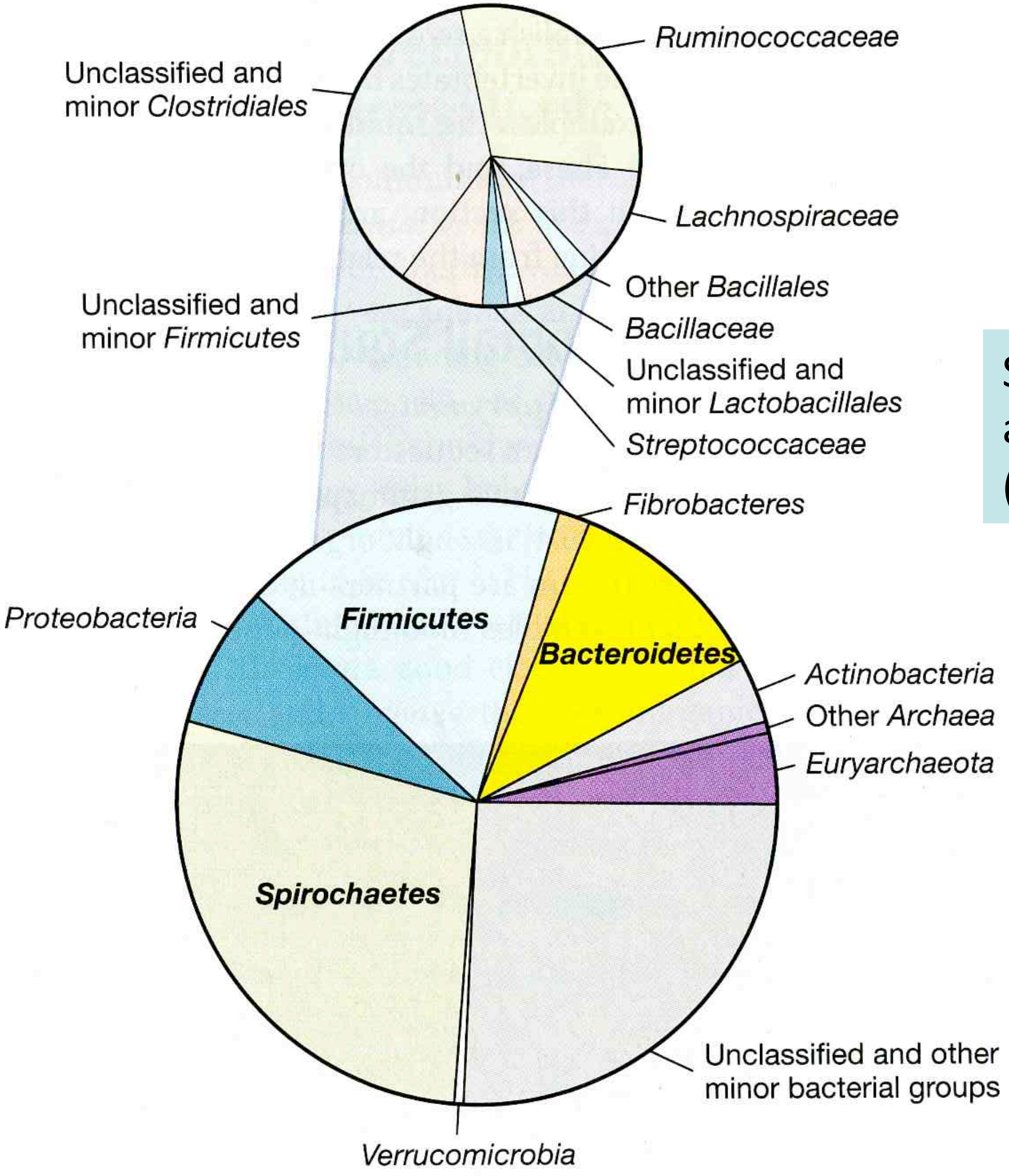
Gut microbiota
Flagellates in lower termites
Bacteria in higher termites

Major microbial processes in the hindgut of termites

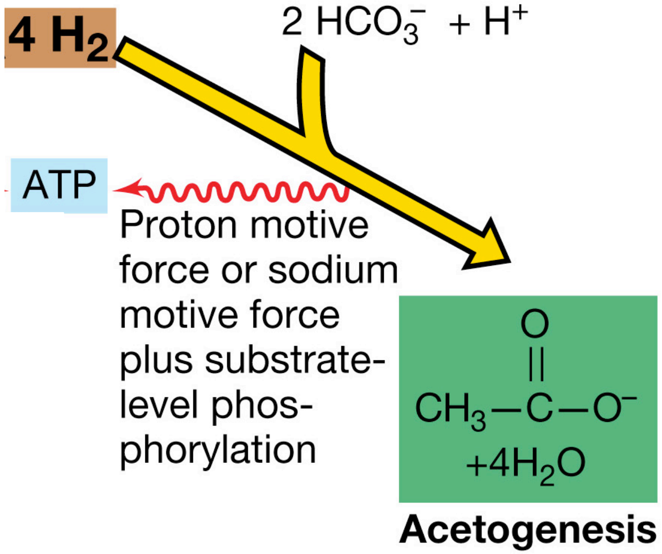




Microbial composition of termite hindgut inferred from 16S rRNA gene sequences



Spirochetes of the genus *Treponema* are the major CO2-reducing acetogens (Acetyl-CoA-pathway) in the hindgut



$4 H_2$

$2 HCO_3^- + H^+$

ATP

Proton motive force or sodium motive force plus substrate-level phosphorylation

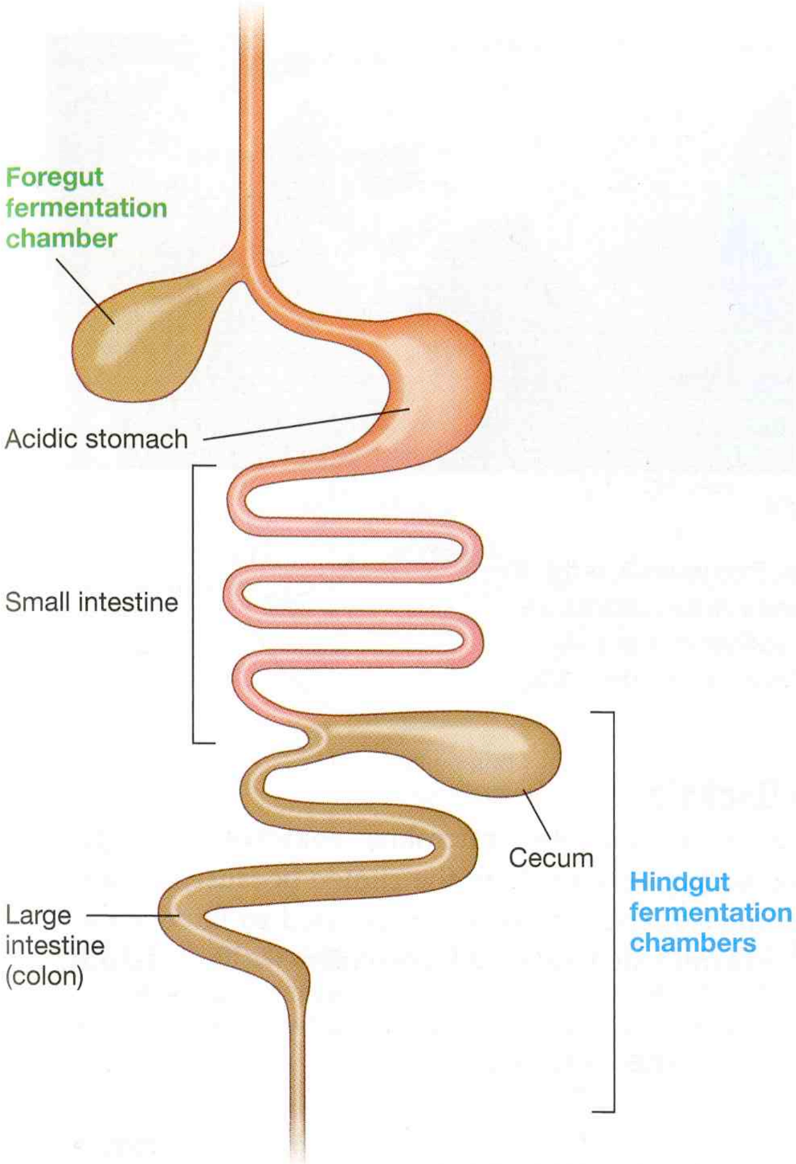
$CH_3-C(=O)-O^-$

$+4H_2O$

Acetogenesis

Mammals as Microbial Habitats

The mammalian gut architecture



Foregut fermenters Examples: Ruminants (photo 1), colobine monkeys, macropod marsupials, hoatzin (photo 2)

1.

2.

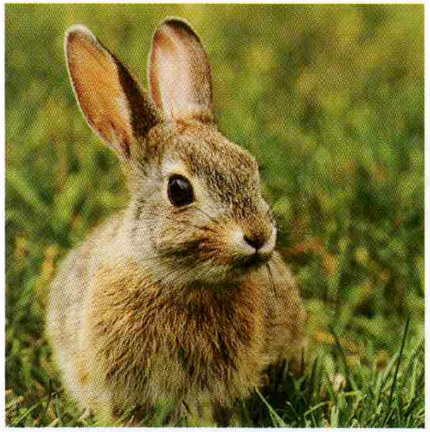
Bernard Swain

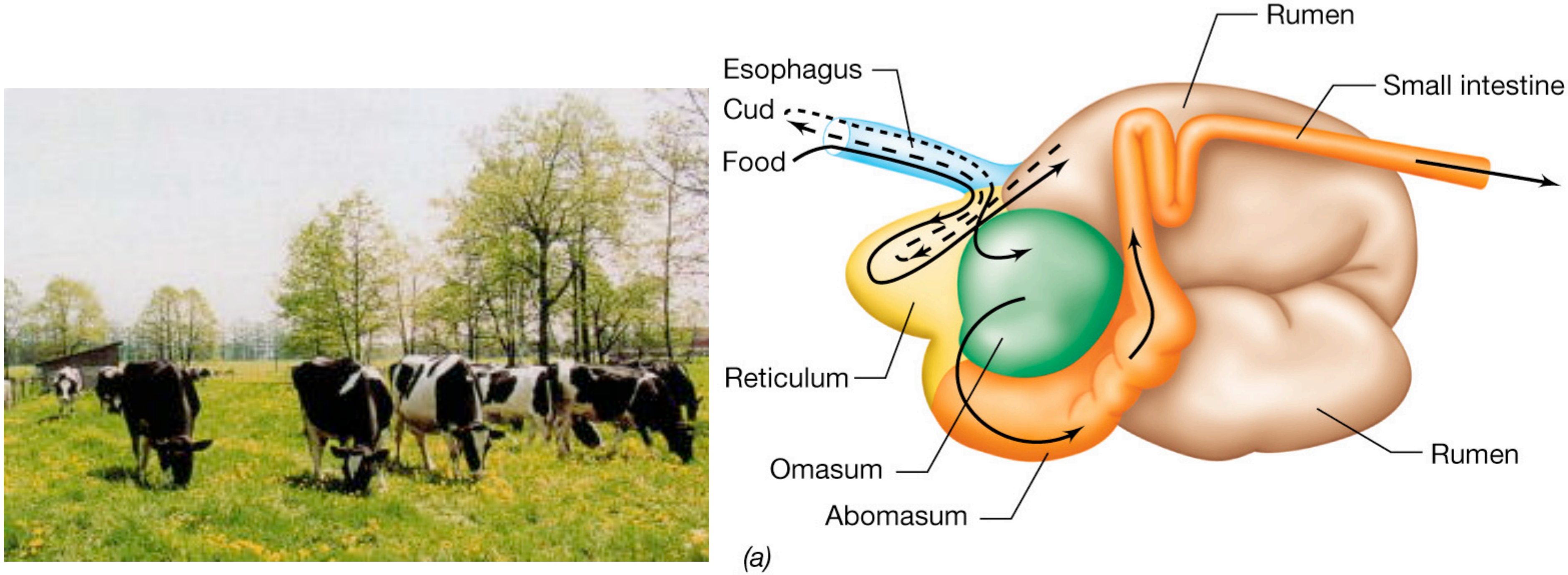
Hindgut fermenters Examples: Cecal animals (photos 3 and 4), primates, some rodents, some reptiles

3.

Nancy L. Spear

4.





(a)

Sharisa D. Beek, Dept. Animal Science, Southern Illinois Univ.

(b)

Ruminal microbial community inferred from 16S rRNA gene

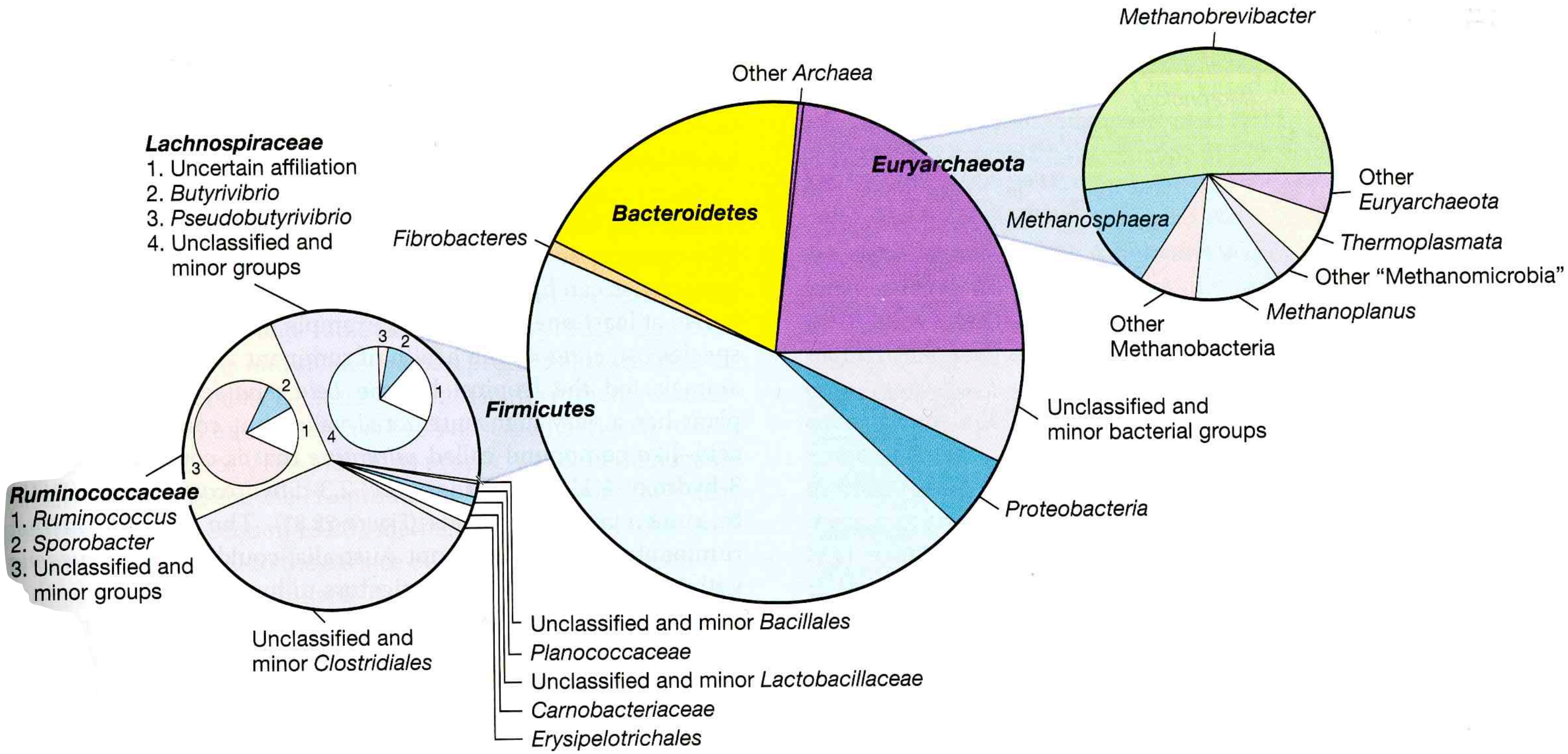
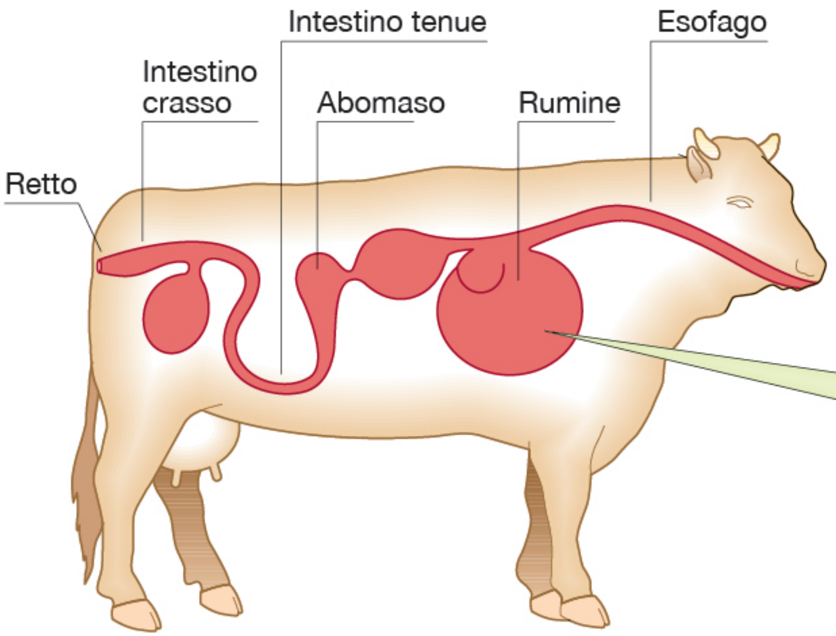


Table 22.2 Characteristics of some rumen prokaryotes

Organism[a]	*Morphology*	*Fermentation products*
Cellulose decomposers		
Gram-negative		
Fibrobacter succinogenes[b]	Rod	Succinate, acetate, formate
Butyrivibrio fibrisolvens[c]	Curved rod	Acetate, formate, lactate, butyrate, H_2, CO_2
Gram-positive		
Ruminococcus albus[c]	Coccus	Acetate, formate, H_2, CO_2
"*Clostridium lochheadii*"	Rod (endospores)	Acetate, formate, butyrate, H_2, CO_2
Starch decomposers		
Gram-negative		
Prevotella ruminicola[d]	Rod	Formate, acetate, succinate
Ruminobacter amylophilus	Rod	Formate, acetate, succinate
Selenomonas ruminantium	Curved rod	Acetate, propionate, lactate
Succinomonas amylolytica	Oval	Acetate, propionate, succinate
Gram-positive		
Streptococcus bovis	Coccus	Lactate
Lactate decomposers		
Gram-negative		
Selenomonas ruminantium subsp. *lactilytica*	Curved rod	Acetate, succinate
Megasphaera elsdenii	Coccus	Acetate, propionate, butyrate, valerate, caproate, H_2, CO_2
Succinate decomposer		
Gram-negative		
Schwartzia succinovorans	Rod	Propionate, CO_2
Pectin decomposer		
Gram-positive		
Lachnospira multipara	Curved rod	Acetate, formate, lactate, H_2, CO_2
Methanogens		
Methanobrevibacter ruminantium	Rod	CH_4 (from $H_2 + CO_2$ or formate)
Methanomicrobium mobile	Rod	CH_4 (from $H_2 + CO_2$ or formate)



RUMINE

Bacteroidetes
- *Prevotella ruminicola*
- *Prevotella bryantil*

Firmicutes
- *Butyrovibrio fibrisolvens*
- *Ruminococcus flavefaciens*
- *Ruminococcus albus*
- *Eubacterium cellulosolvens*

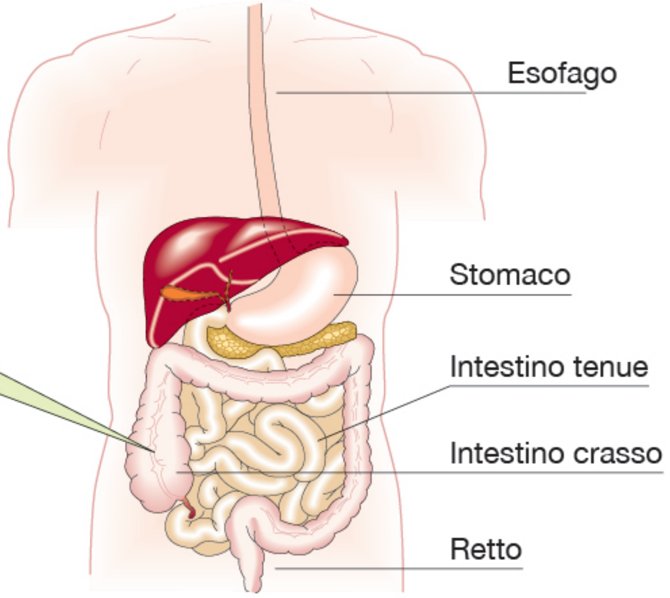
Fibrobacter
- *Fibrobacter succinogenes*
- *Fibrobacter intestinalis*

INTESTINO CRASSO UMANO

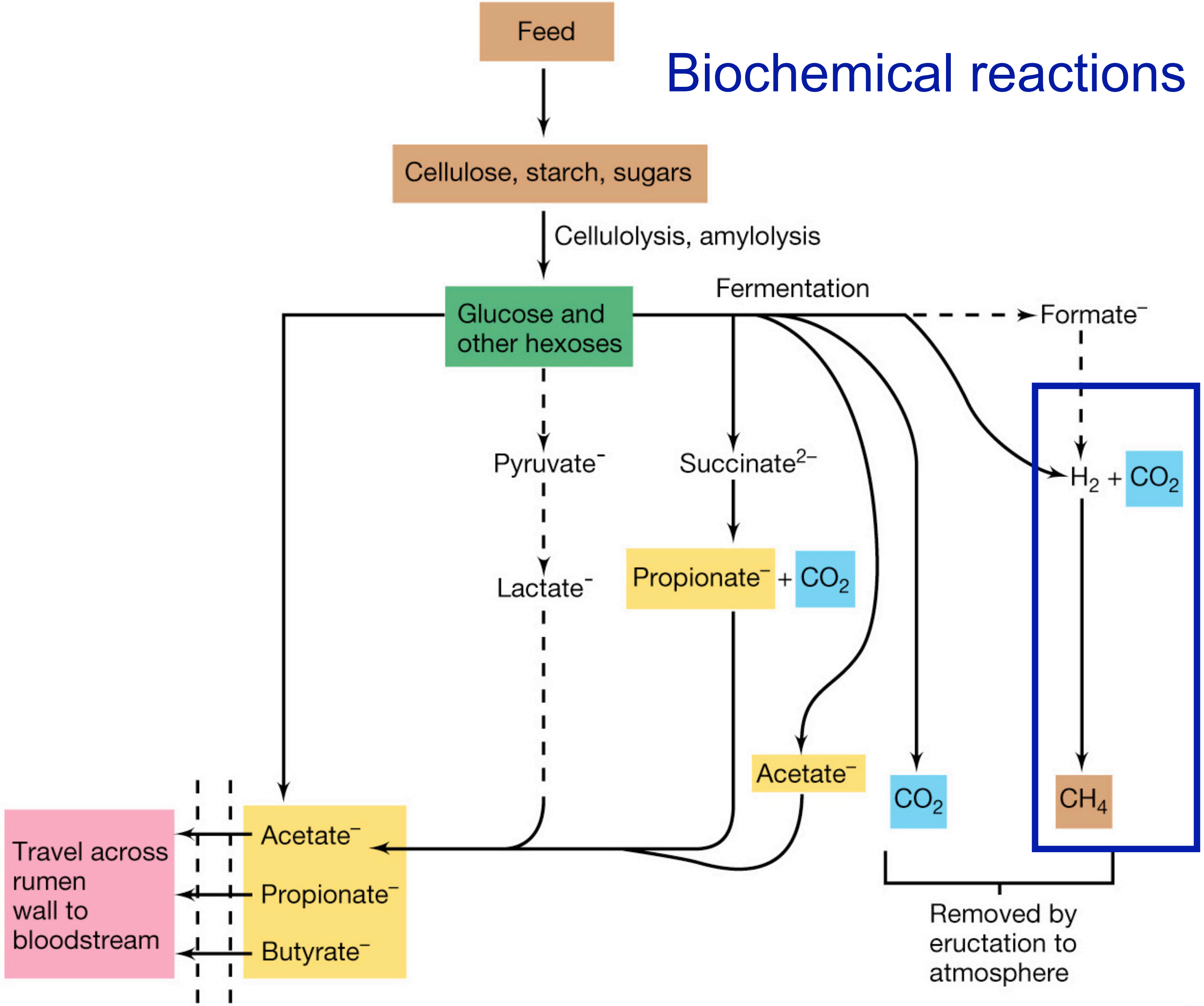
Bacteroidetes
- *Bacteroides thetaiotaomicron*
- *Bacteroides ovatus*
- *Bacteroides cellulosoliticus*
- *Bacteroides* sp. nov.

Firmicutes
- *Roseburia intestinalis*
- *Roseburia inulinivorans*
- *Ruminococcus bromii*
- *Ruminococcus* sp. nov.
- *Eubacterium rectale*

Actinobacteria
- *Bifidobacterium adolescentis*



Biochemical reactions in the rumen

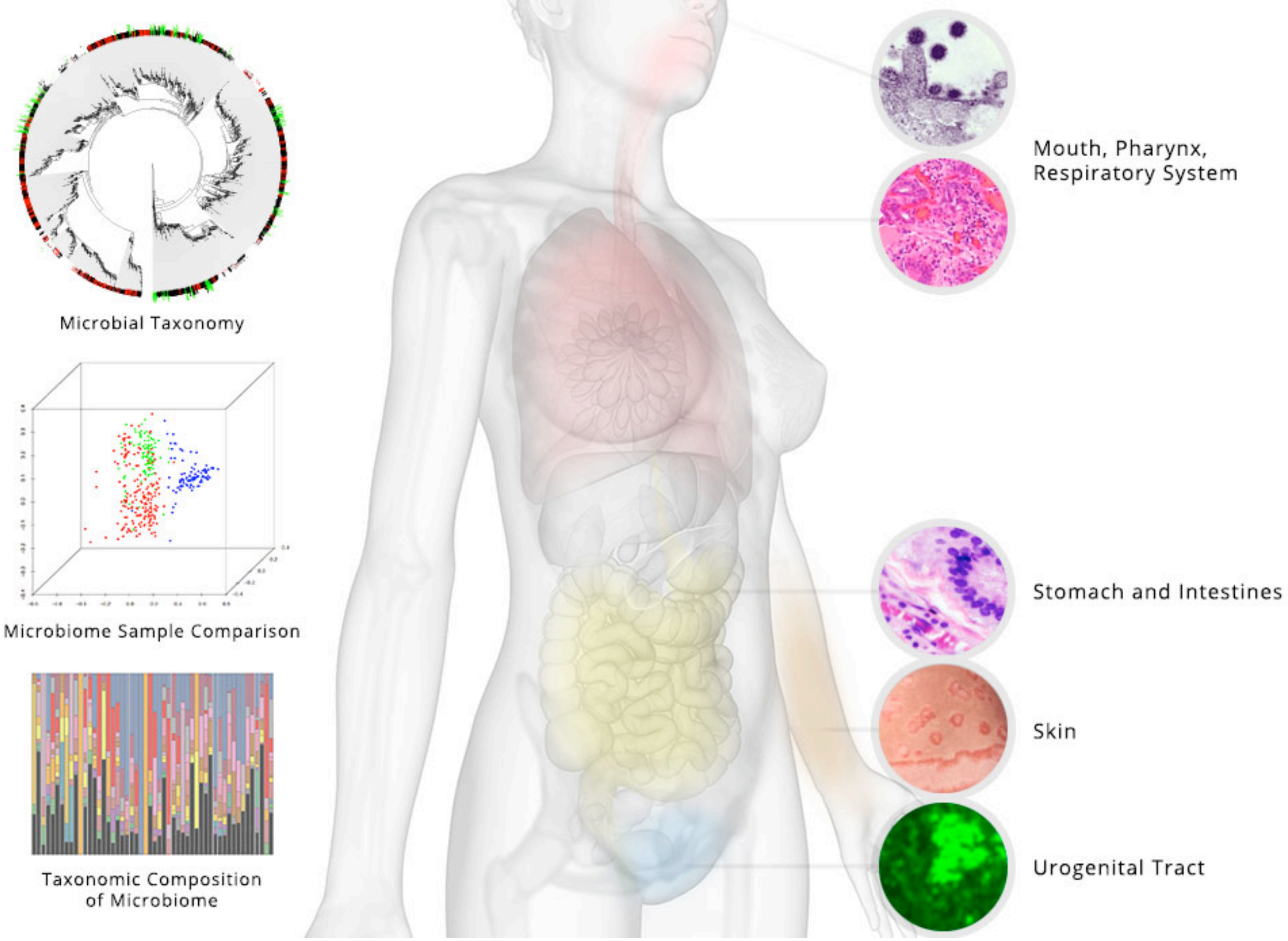


Overall stoichiometry of rumen fermentation:

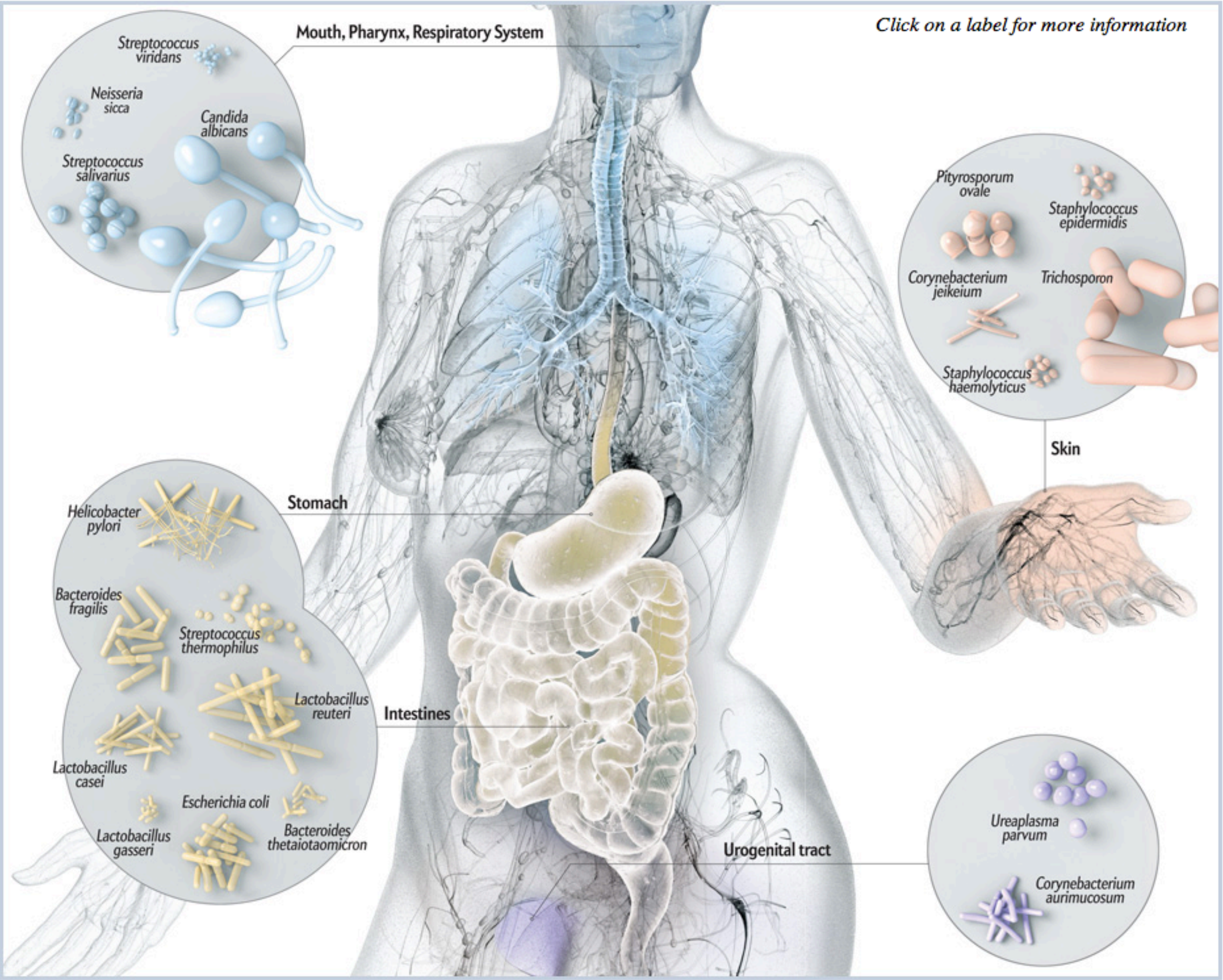
57.5 glucose ⟶ 65 acetate$^-$ + 20 propionate$^-$ + 15 butyrate$^-$ + 60 CO_2 + 35 CH_4 + 25 H_2O

Normal human-microbial interactions

The human microbiome



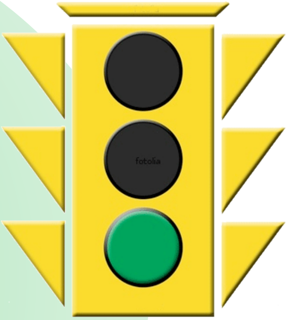
A **microbiota** is the community of commensal, symbiotic and pathogenic microorganism of our body. **Microbiome** and **microbiota** describe either the collective genomes of the microorganisms that reside in an environmental niche or the microorganisms themselves, respectively. However, by the original defonitions these terms are largely synonymous



Relationships among bacteria and humans

The associations are, for the most part, **mutualistics**

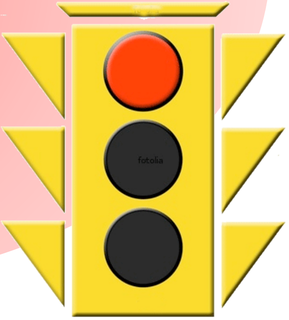
BENEFITS:



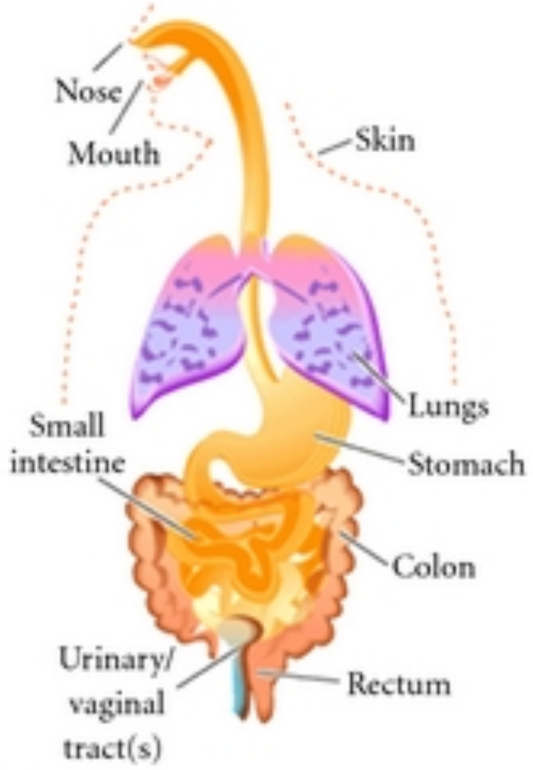
- ✓ Nutrients (Vit B, Vit K)
- ✓ Antigenic stimulation(IgA)
- ✓ Colonization strategy: exclusion of pathogens

DISADVANTAGES:

- ✓ Immunosuppression
- ✓ Change of district
- ✓ Dismicrobism



Microbiota and Microbiome of Human Body



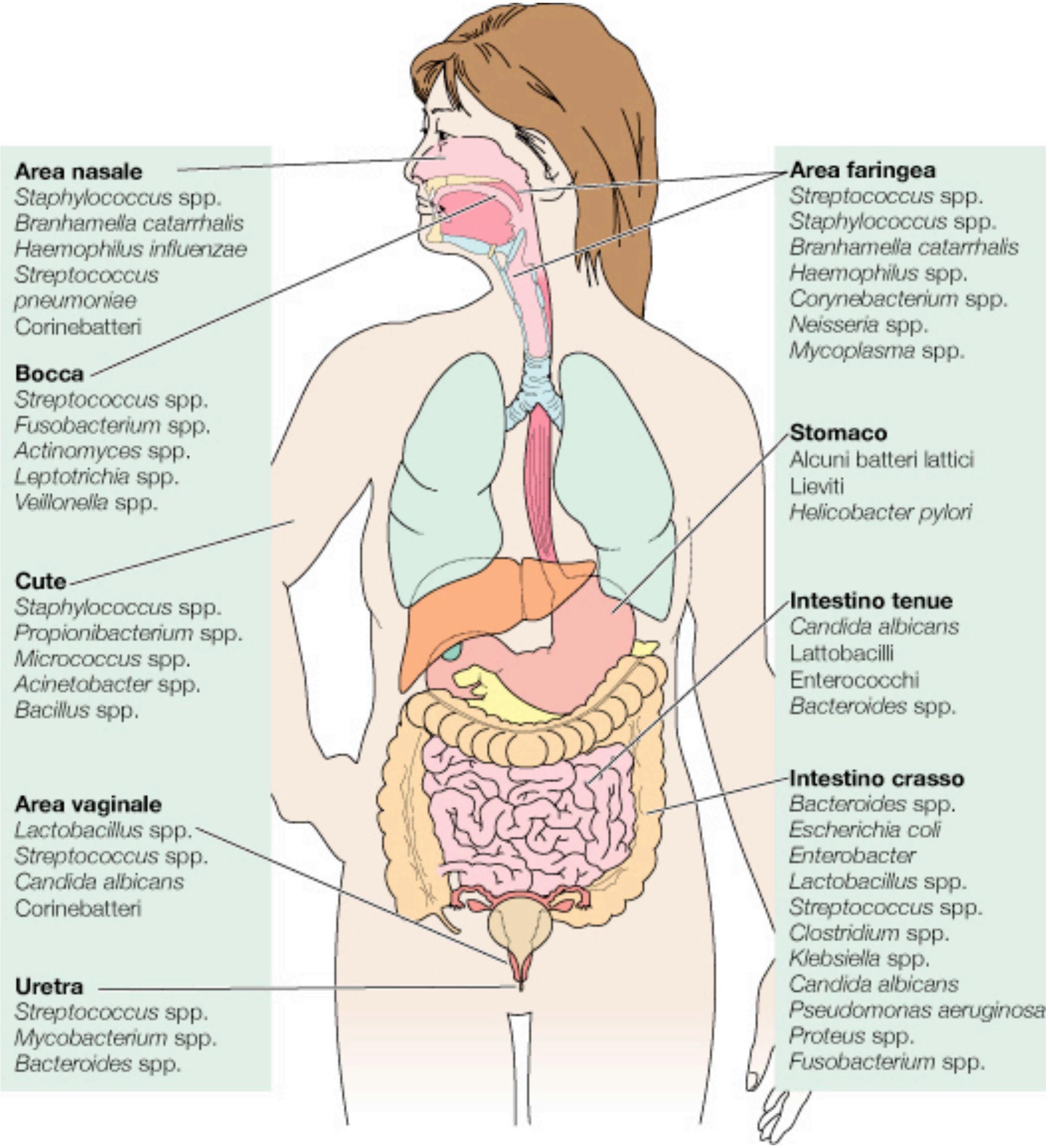
Human body 10^{13} cells 23,000 genes ↔ Normal flora 10^{14} microbial cells on the human body. 3.3 million genes

Amount of bacteria per gram of cellular component

- Stomach – 10^{1} to 10^{2} cells
- Duodenum – 10^{3} cells
- Jejunum – 10^{4} cells
- Ileum 10^{4} to 10^{7} cells
- Proximal colon 10^{10} to 10^{11} cells
- Transverse colon 10^{11} to 10^{12} cells
- Distal colon $>10^{12}$ cells

> "the microbiota can be viewed as a metabolic organ exquisitely tuned to our physiology that performs function we have not had to evolve on our own"
>
> Backhed et al. 2004. PNAS 101:15718-15723

The human microbiota



Area nasale
Staphylococcus spp.
Branhamella catarrhalis
Haemophilus influenzae
Streptococcus pneumoniae
Corinebatteri

Bocca
Streptococcus spp.
Fusobacterium spp.
Actinomyces spp.
Leptotrichia spp.
Veillonella spp.

Cute
Staphylococcus spp.
Propionibacterium spp.
Micrococcus spp.
Acinetobacter spp.
Bacillus spp.

Area vaginale
Lactobacillus spp.
Streptococcus spp.
Candida albicans
Corinebatteri

Uretra
Streptococcus spp.
Mycobacterium spp.
Bacteroides spp.

Area faringea
Streptococcus spp.
Staphylococcus spp.
Branhamella catarrhalis
Haemophilus spp.
Corynebacterium spp.
Neisseria spp.
Mycoplasma spp.

Stomaco
Alcuni batteri lattici
Lieviti
Helicobacter pylori

Intestino tenue
Candida albicans
Lattobacilli
Enterococchi
Bacteroides spp.

Intestino crasso
Bacteroides spp.
Escherichia coli
Enterobacter
Lactobacillus spp.
Streptococcus spp.
Clostridium spp.
Klebsiella spp.
Candida albicans
Pseudomonas aeruginosa
Proteus spp.
Fusobacterium spp.

- ✓ Age
- ✓ Diet
- ✓ Hormonal status
- ✓ State of health
- ✓ Personal hygiene

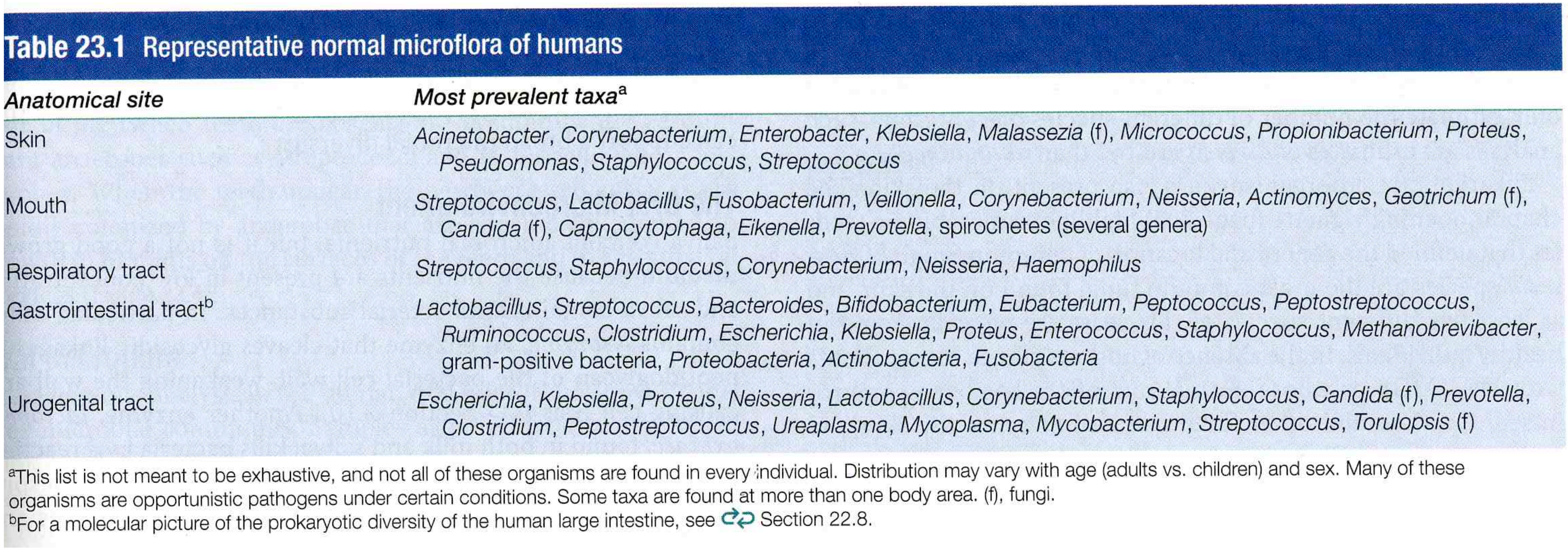


Table 23.1 Representative normal microflora of humans

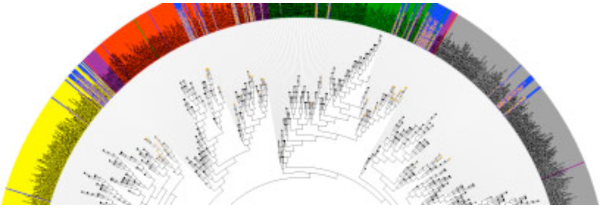
Anatomical site	*Most prevalent taxa*[a]
Skin	*Acinetobacter*, *Corynebacterium*, *Enterobacter*, *Klebsiella*, *Malassezia* (f), *Micrococcus*, *Propionibacterium*, *Proteus*, *Pseudomonas*, *Staphylococcus*, *Streptococcus*
Mouth	*Streptococcus*, *Lactobacillus*, *Fusobacterium*, *Veillonella*, *Corynebacterium*, *Neisseria*, *Actinomyces*, *Geotrichum* (f), *Candida* (f), *Capnocytophaga*, *Eikenella*, *Prevotella*, spirochetes (several genera)
Respiratory tract	*Streptococcus*, *Staphylococcus*, *Corynebacterium*, *Neisseria*, *Haemophilus*
Gastrointestinal tract[b]	*Lactobacillus*, *Streptococcus*, *Bacteroides*, *Bifidobacterium*, *Eubacterium*, *Peptococcus*, *Peptostreptococcus*, *Ruminococcus*, *Clostridium*, *Escherichia*, *Klebsiella*, *Proteus*, *Enterococcus*, *Staphylococcus*, *Methanobrevibacter*, gram-positive bacteria, *Proteobacteria*, *Actinobacteria*, *Fusobacteria*
Urogenital tract	*Escherichia*, *Klebsiella*, *Proteus*, *Neisseria*, *Lactobacillus*, *Corynebacterium*, *Staphylococcus*, *Candida* (f), *Prevotella*, *Clostridium*, *Peptostreptococcus*, *Ureaplasma*, *Mycoplasma*, *Mycobacterium*, *Streptococcus*, *Torulopsis* (f)

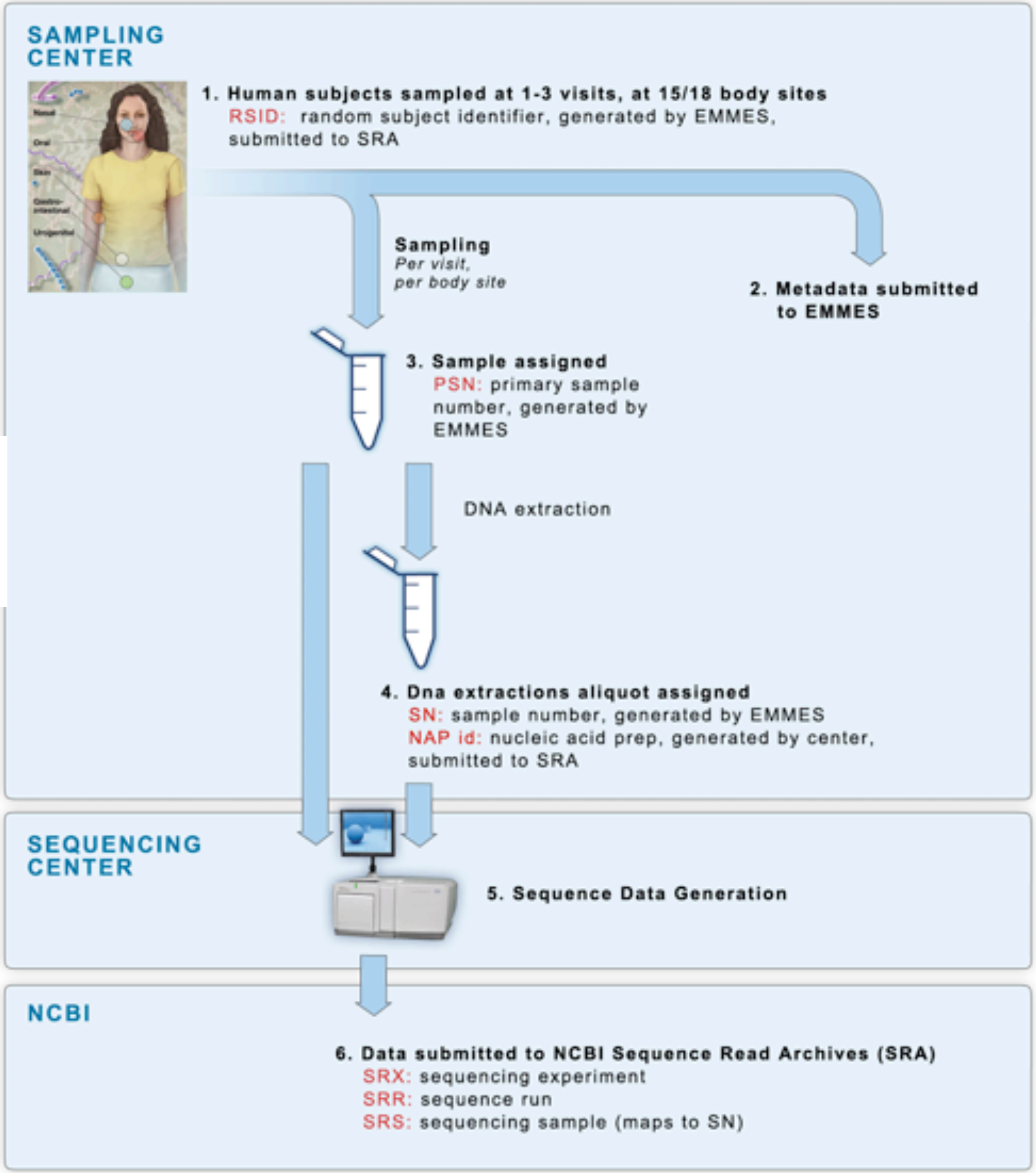
[a] This list is not meant to be exhaustive, and not all of these organisms are found in every individual. Distribution may vary with age (adults vs. children) and sex. Many of these organisms are opportunistic pathogens under certain conditions. Some taxa are found at more than one body area. (f), fungi.

[b] For a molecular picture of the prokaryotic diversity of the human large intestine, see Section 22.8.

"The human microbiota consists of the 10-100 trillion symbiotic microbial cells harbored by each person, primarily bacteria in the gut; the human microbiome consists of the genes these cells harbor" (Nature, 2012)

NIH HUMAN
MICROBIOME
PROJECT





SAMPLING CENTER

1. Human subjects sampled at 1-3 visits, at 15/18 body sites
RSID: random subject identifier, generated by EMMES, submitted to SRA

Sampling
Per visit, per body site

2. Metadata submitted to EMMES

3. Sample assigned
PSN: primary sample number, generated by EMMES

DNA extraction

4. Dna extractions aliquot assigned
SN: sample number, generated by EMMES
NAP id: nucleic acid prep, generated by center, submitted to SRA

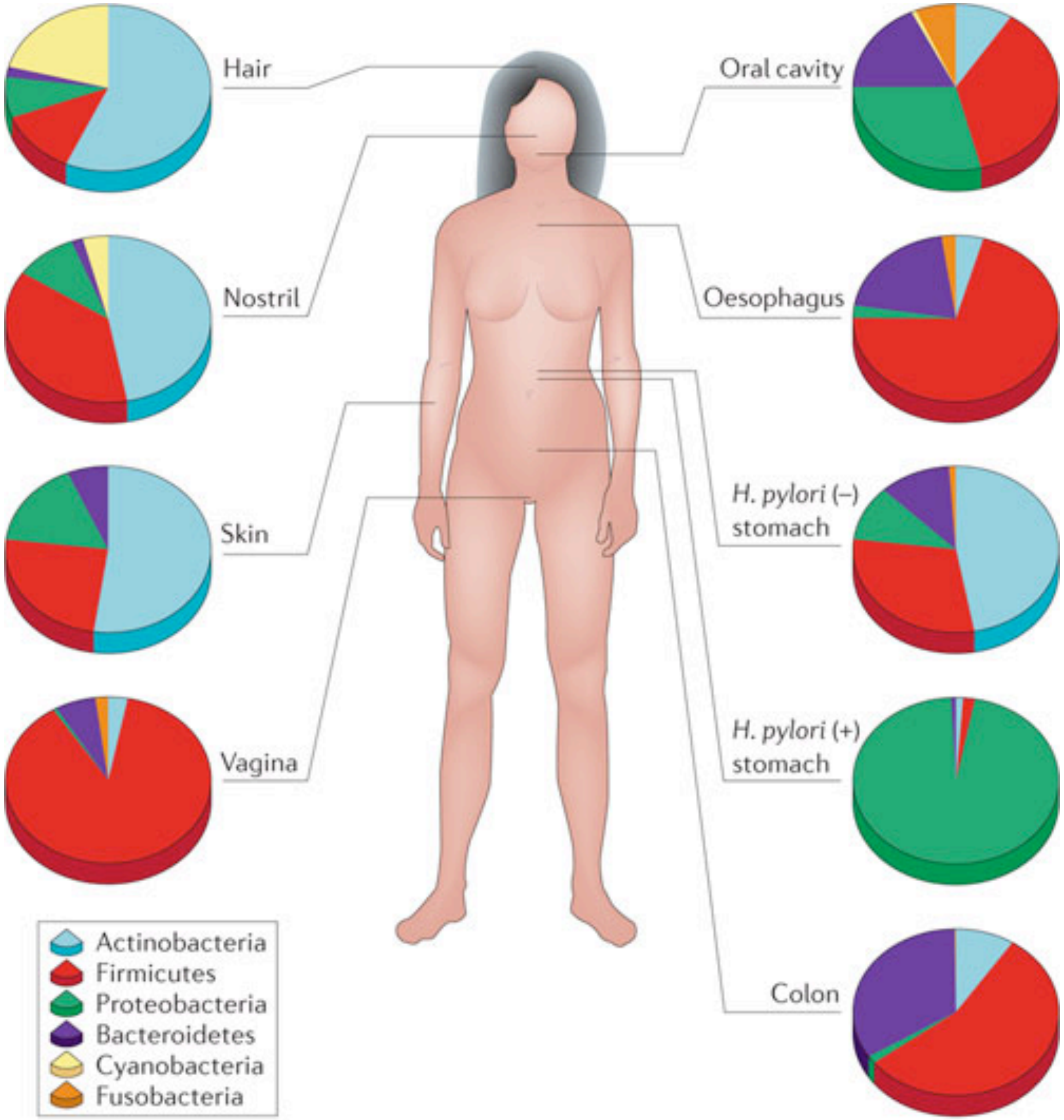
SEQUENCING CENTER

5. Sequence Data Generation

NCBI

6. Data submitted to NCBI Sequence Read Archives (SRA)
SRX: sequencing experiment
SRR: sequence run
SRS: sequencing sample (maps to SN)

Compositional differences in the microbiome by anatomical site



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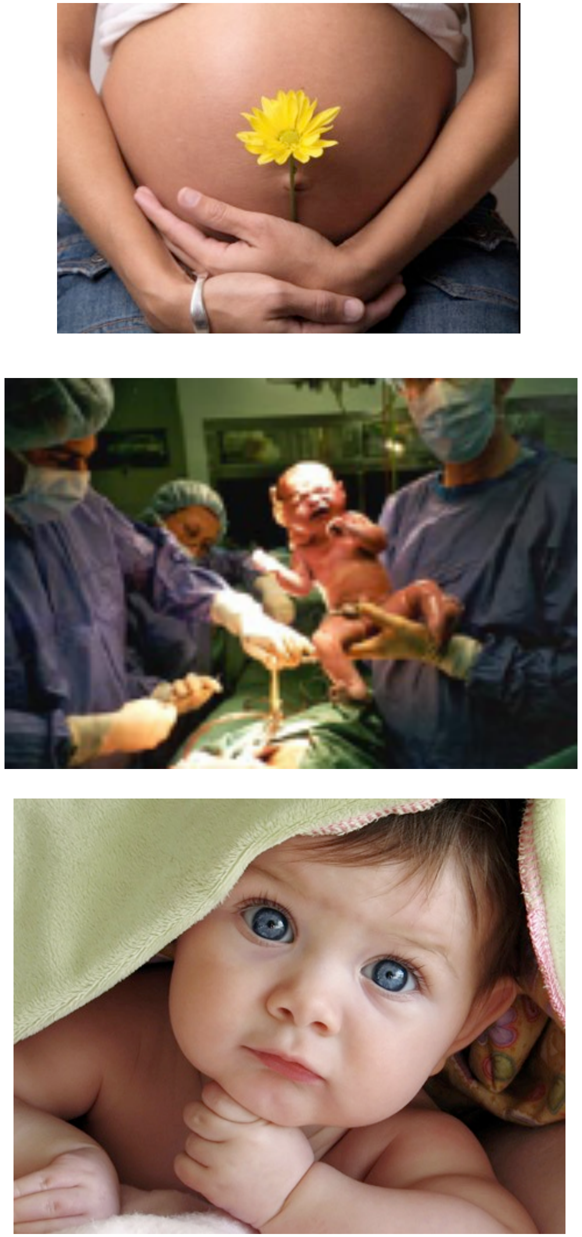
Acquisition of the microbiome in early life

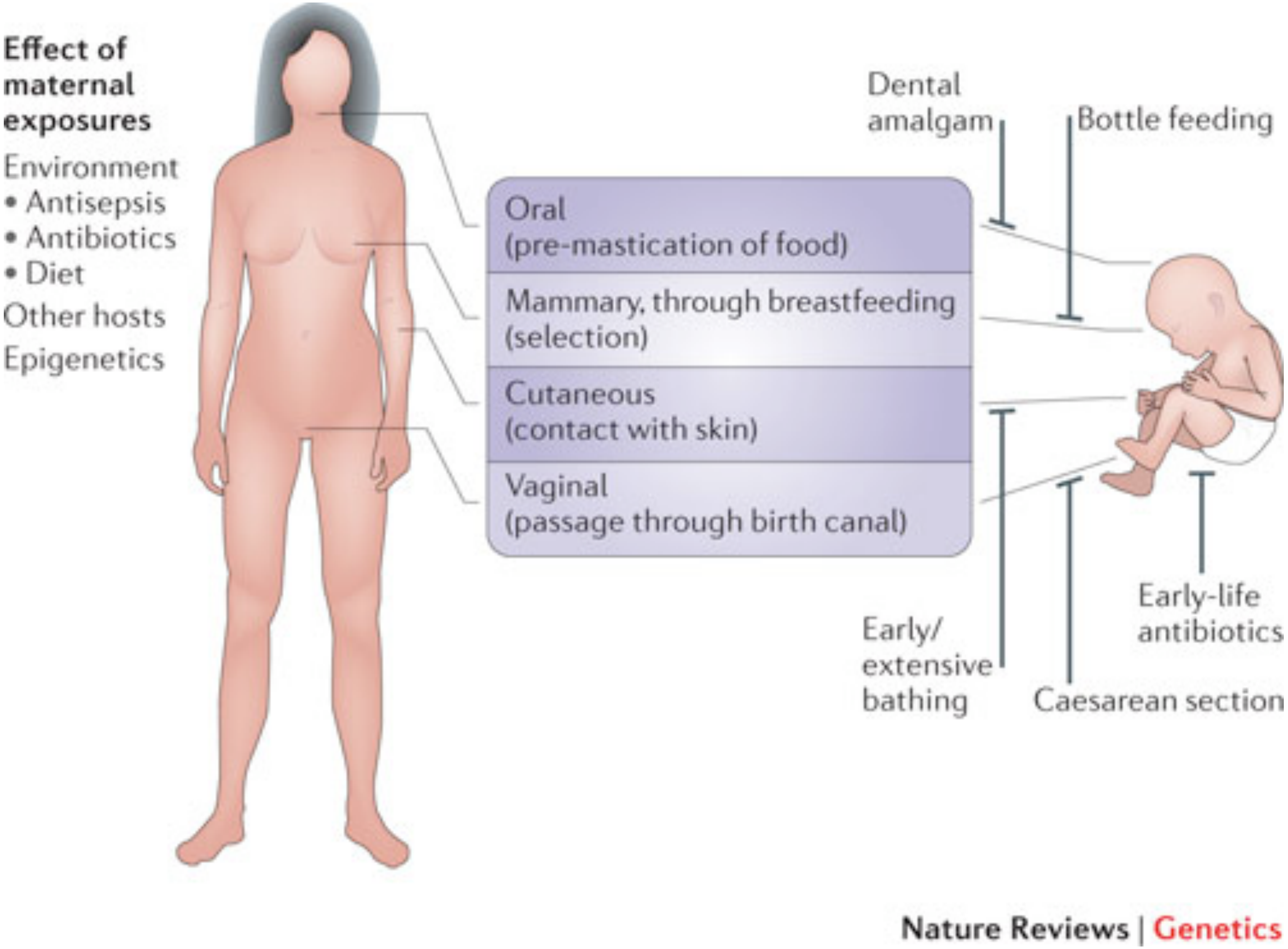


FETUS = STERILE

First colonization occurs:

- ✓ through the birth canal;
- ✓ first breaths;
- ✓ operators' hands;
- ✓ food ingestion.

Acquisition of the microbiome in early life by vertical transmission, and factors modifying mother-to-child microbial transmission



Effect of maternal exposures

Environment
- Antisepsis
- Antibiotics
- Diet

Other hosts

Epigenetics

Oral
(pre-mastication of food)

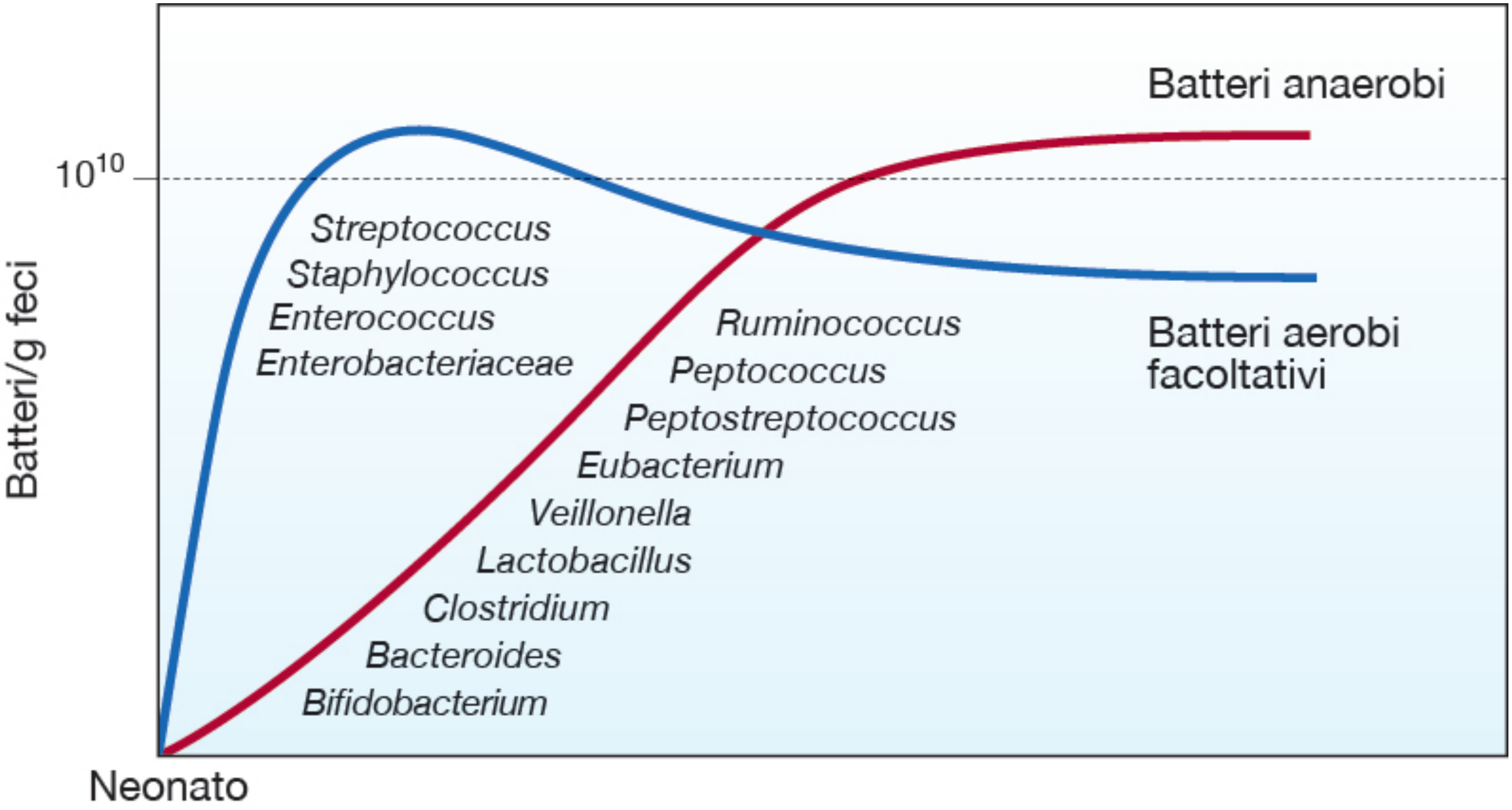
Mammary, through breastfeeding
(selection)

Cutaneous
(contact with skin)

Vaginal
(passage through birth canal)

Nature Reviews | Genetics

Acquisition of the gut microbiome in early life



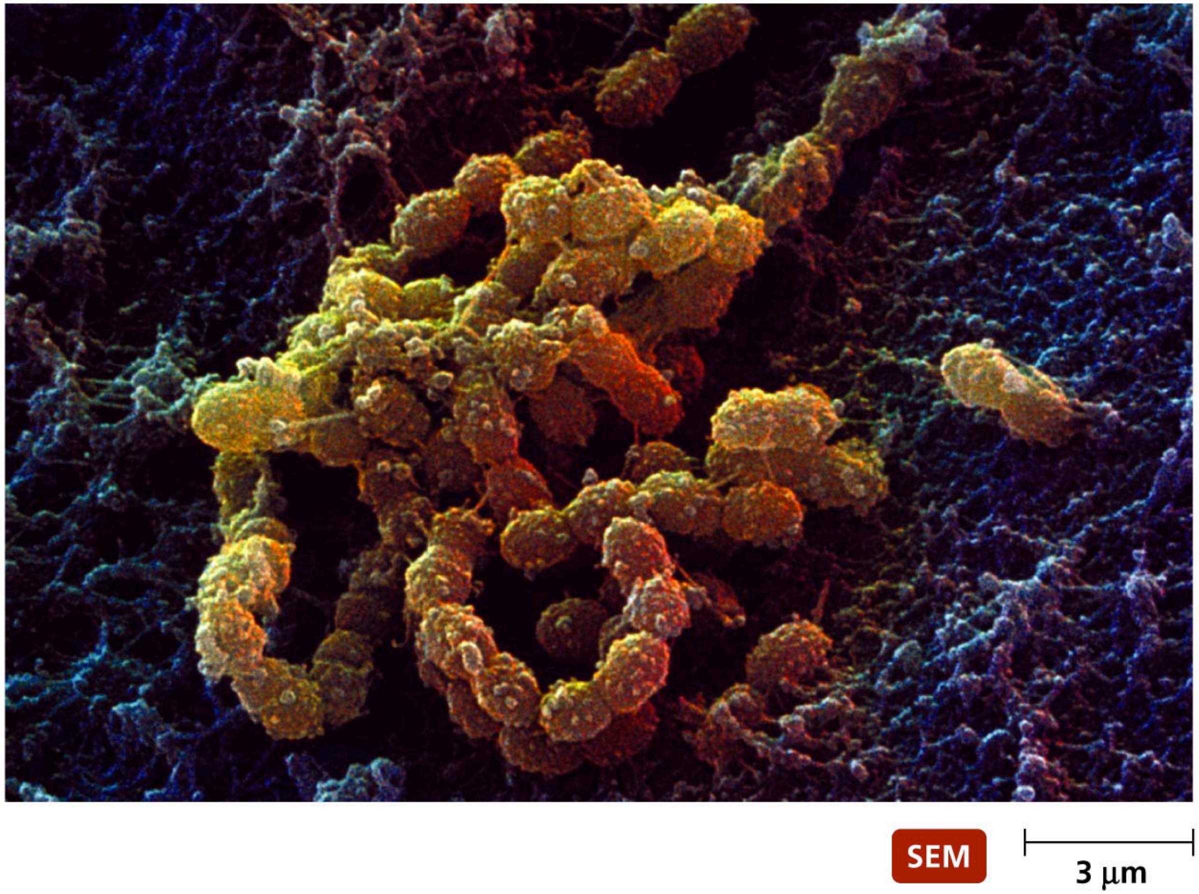
The human microbiota: general features

- Microorganisms of the normal flora exhibits tissue preferences or predilection for colonization (tissue tropism)
- Many of them are able to specifically colonize a particular tissue or surface using their own surface components (e.g. capsules, fimbriae, pili, cell wall components, EPS) as specific ligands for attachment to **specific receptors** located at the colonization site.

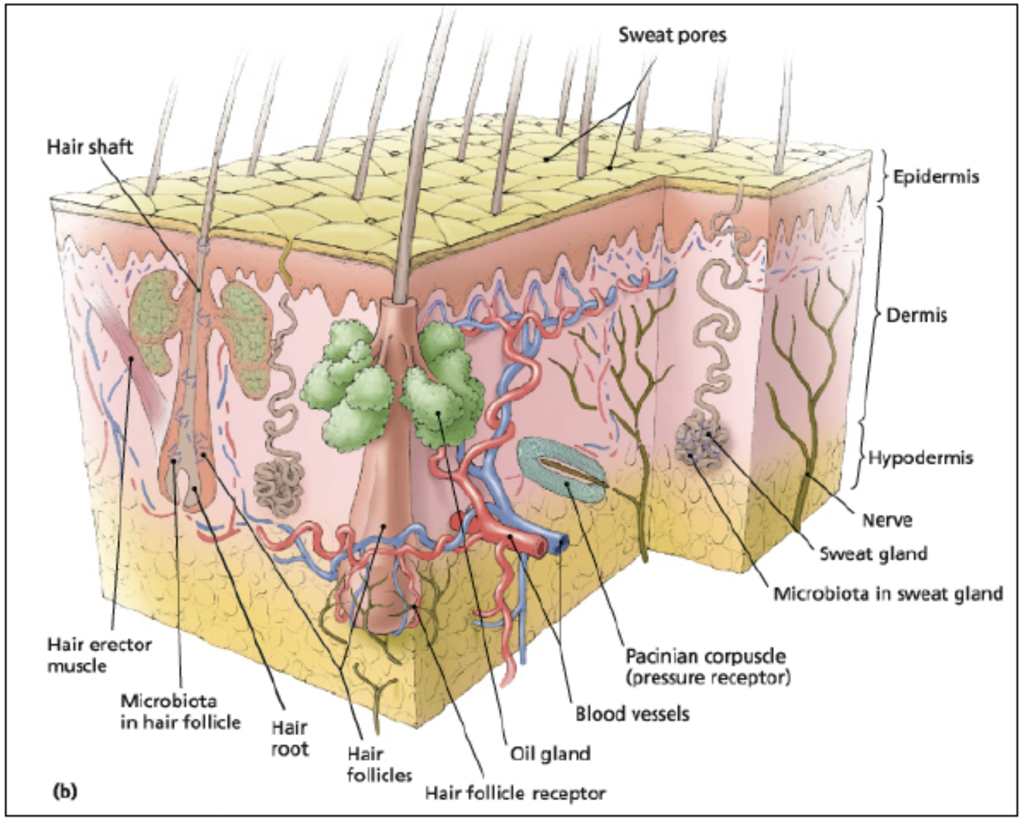
S. pyogenes	Protein F	Amino terminus of fibronectin	Pharyngeal epithelium
S. mutans	Glycosyl transferase	Salivary glycoprotein	Pellicle of tooth
S. pneumoniae	Cell-bound protein	N-acetylhexosamine-galactose disaccharide	Mucosal epithelium
S. aureus	Cell-bound protein	Amino terminus of fibronectin	Mucosal epithelium
Enterotoxigenic *E. coli*	Type-1 fimbriae	Species-specific carbohydrate(s)	Intestinal epithelium
Uropathogenic *E. coli*	Type 1 fimbriae	Complex carbohydrate	Urethral epithelium
Uropathogenic *E. coli*	P-pili (pap)	Globobiose linked to ceramide lipid	Upper urinary tract
B. pertussis	Fimbriae ("filamentous hemagglutinin")	Galactose on sulfated glycolipids	Respiratory epithelium
V. cholerae	N-methylphenylalanine pili	Fucose and mannose	Intestinal epithelium

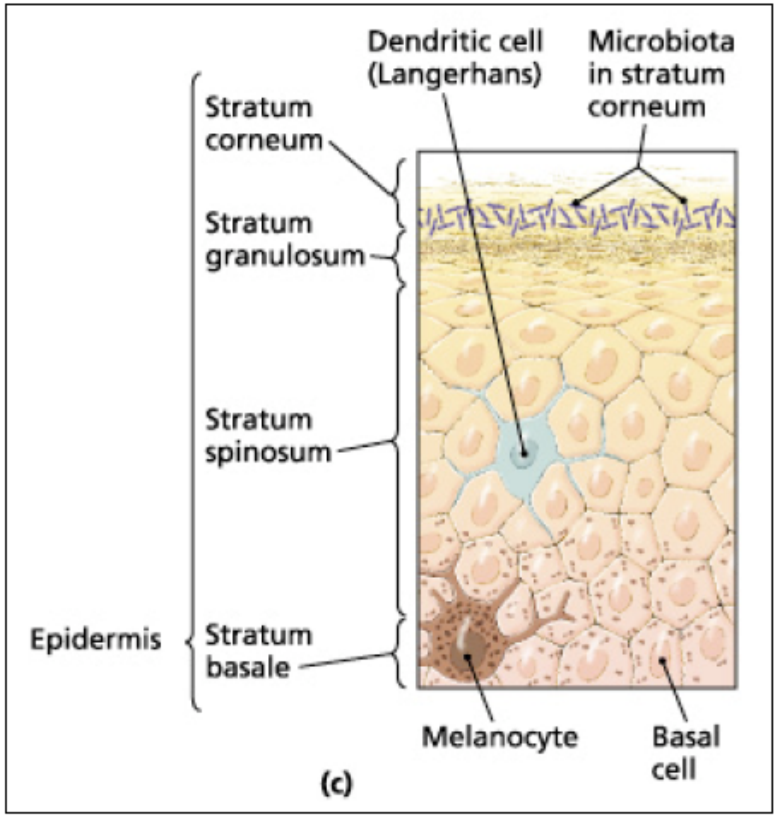
The human microbiota: general features

- ✓ Some bacteria of the microbiota are able to construct biofilms on tissue surface or they are able to colonized a biofilm built by another bacterial species (e.g. dental plaque)



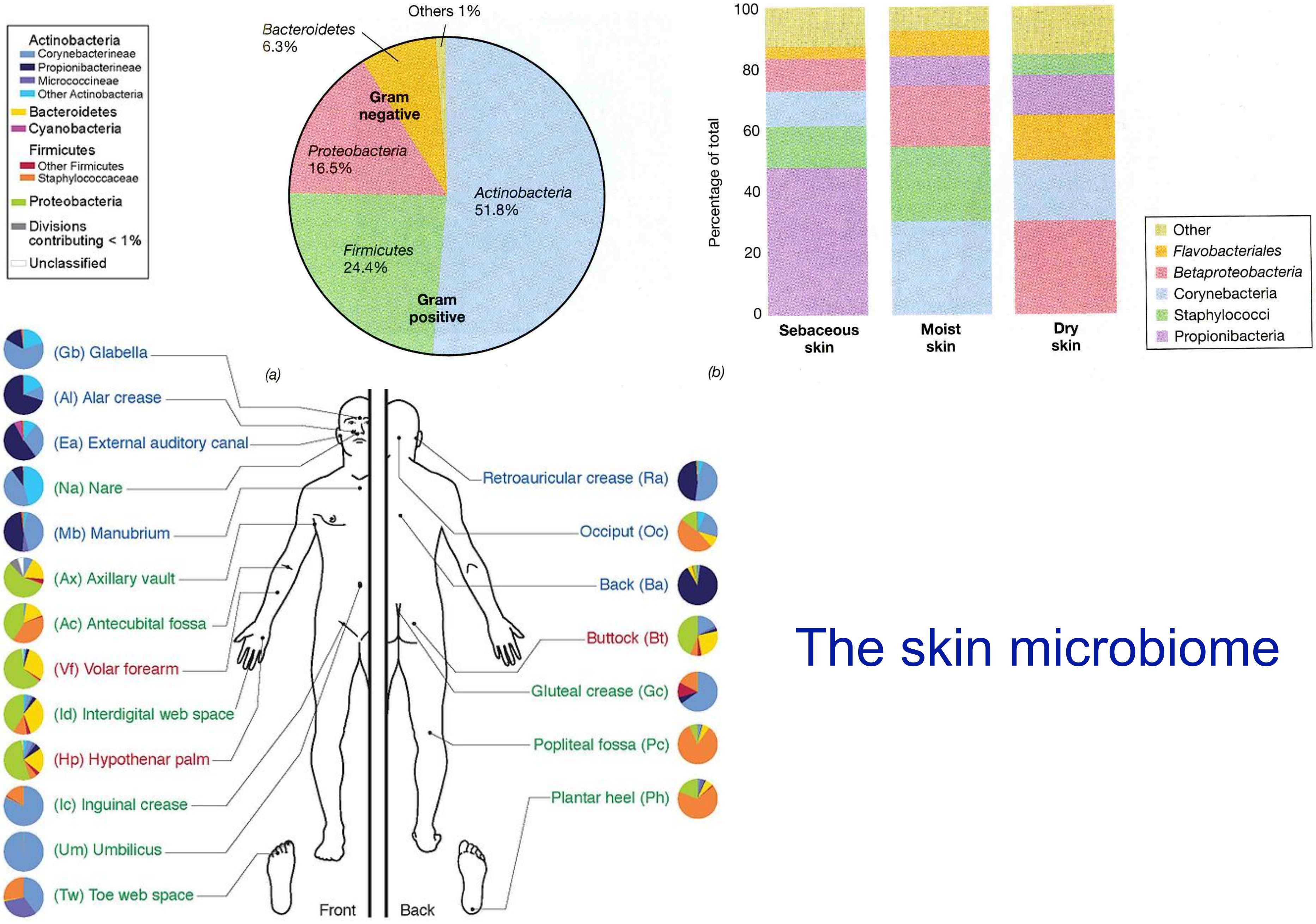
The skin microbiota





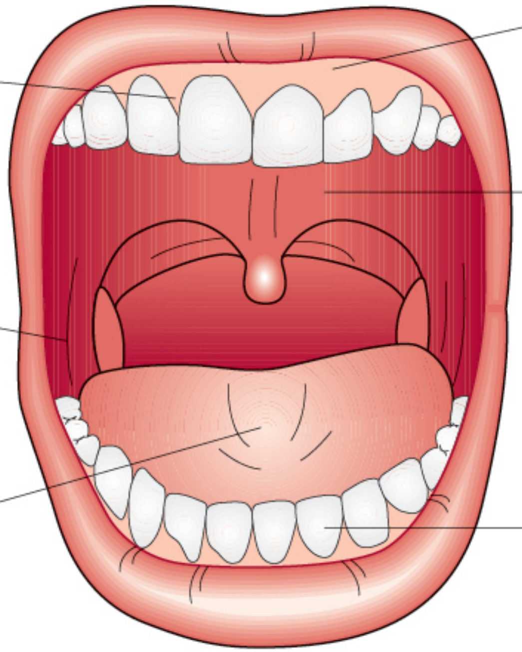
TRANSIENT >>> **RESIDENT**

- ✓ pH: acid 4-6
- ✓ Dry environment
- ✓ High NaCl concentration
- ✓ Inhibitory substances (lysozyme, lipids)



The skin microbiome

Microbiota of the oral cavity



Interstizi gengivali
(streptococchi
Actinomyces spp.,
cocchi e bastoncelli
Gram negativi anaerobi,
cocchi e bastoncelli
Gram positivi anaerobi)

Guancia
(streptococchi,
Actinomyces spp.,
Haemophilus spp.)

Lingua
(streptococchi,
Haemophilus spp.,
Veillonella spp.)

Gengiva
(streptococchi,
Actinomyces sp

Palato
(streptococchi,
Actinomyces sp

Superficie dentale
(molto complessa,
streptococchi,
Actinomyces spp.
Veillonella spp.,
Fusobacterium spp.)

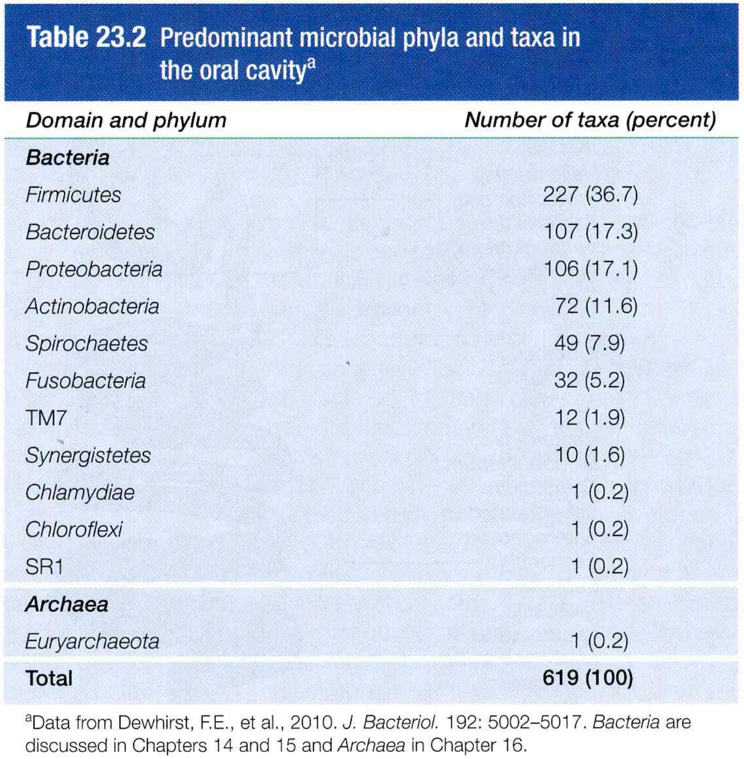
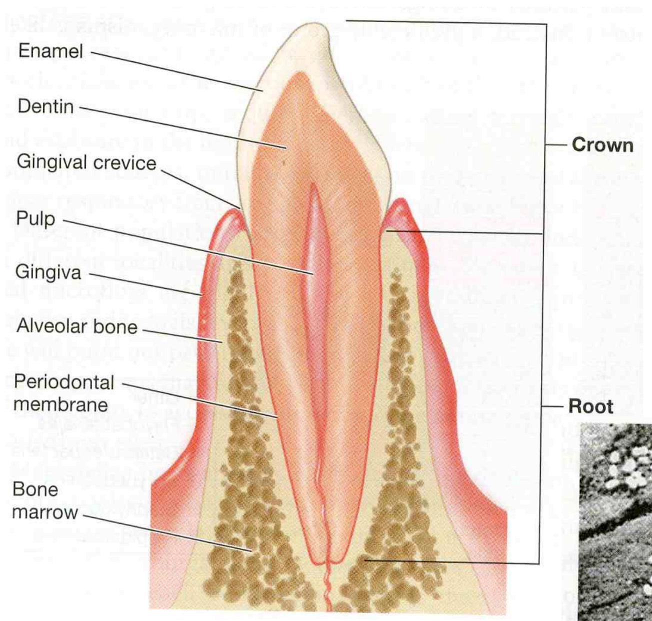


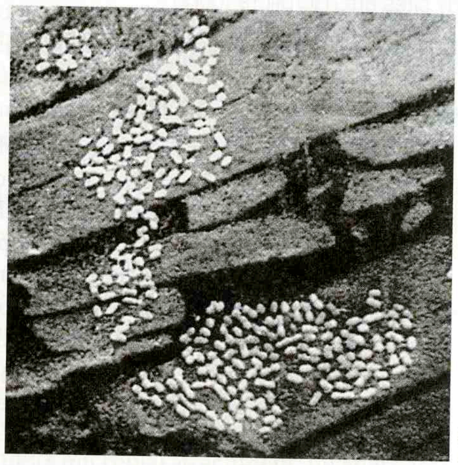
Table 23.2 Predominant microbial phyla and taxa in the oral cavity[a]

Domain and phylum	*Number of taxa (percent)*
Bacteria	
Firmicutes	227 (36.7)
Bacteroidetes	107 (17.3)
Proteobacteria	106 (17.1)
Actinobacteria	72 (11.6)
Spirochaetes	49 (7.9)
Fusobacteria	32 (5.2)
TM7	12 (1.9)
Synergistetes	10 (1.6)
Chlamydiae	1 (0.2)
Chloroflexi	1 (0.2)
SR1	1 (0.2)
Archaea	
Euryarchaeota	1 (0.2)
Total	**619 (100)**

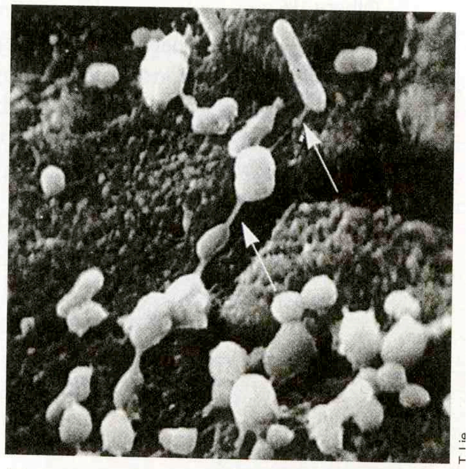
[a] Data from Dewhirst, F.E., et al., 2010. *J. Bacteriol.* 192: 5002–5017. *Bacteria* are discussed in Chapters 14 and 15 and *Archaea* in Chapter 16.

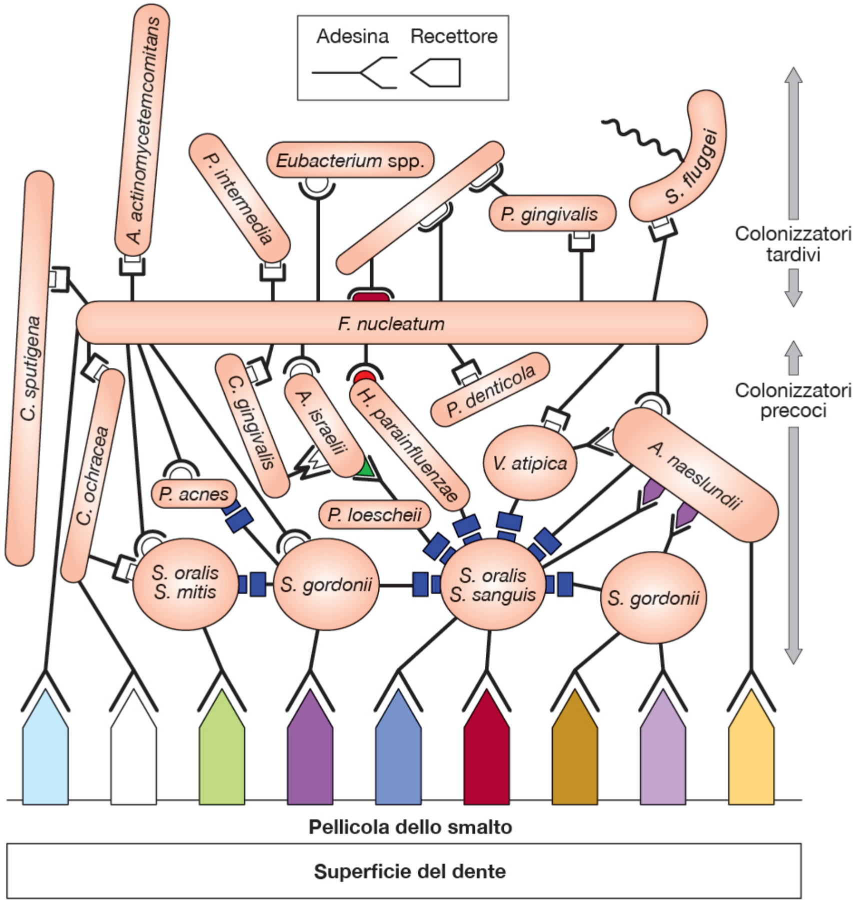
The Dental Plaque





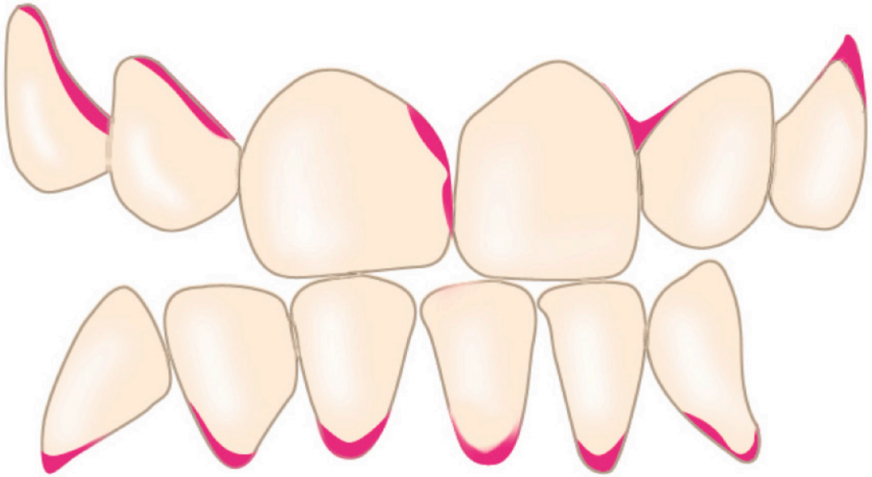
(a)



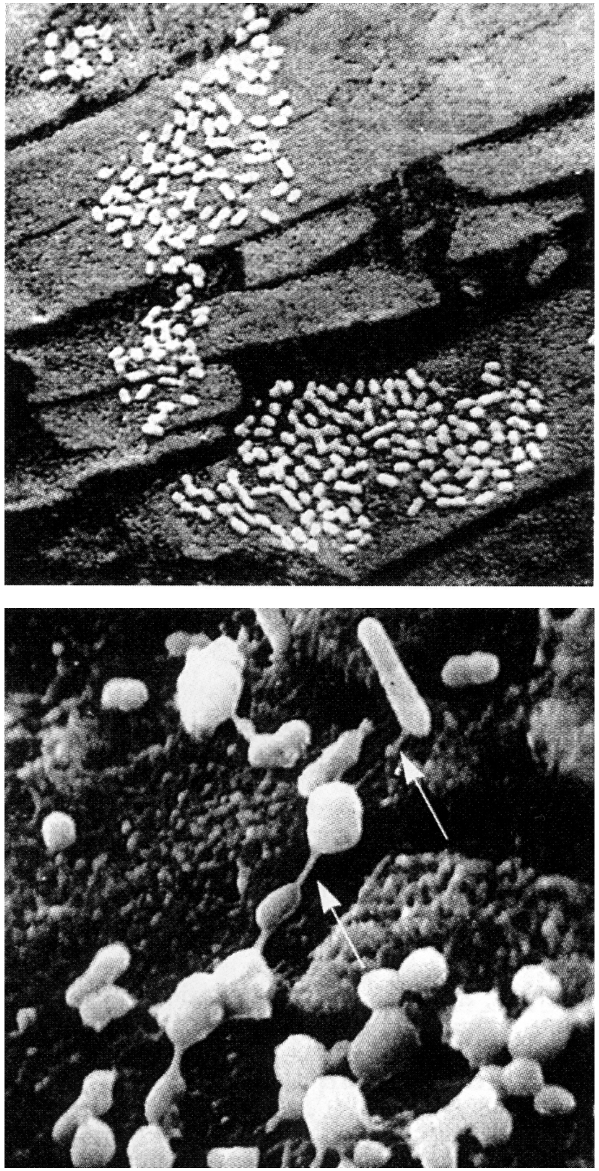


The Dental Plaque

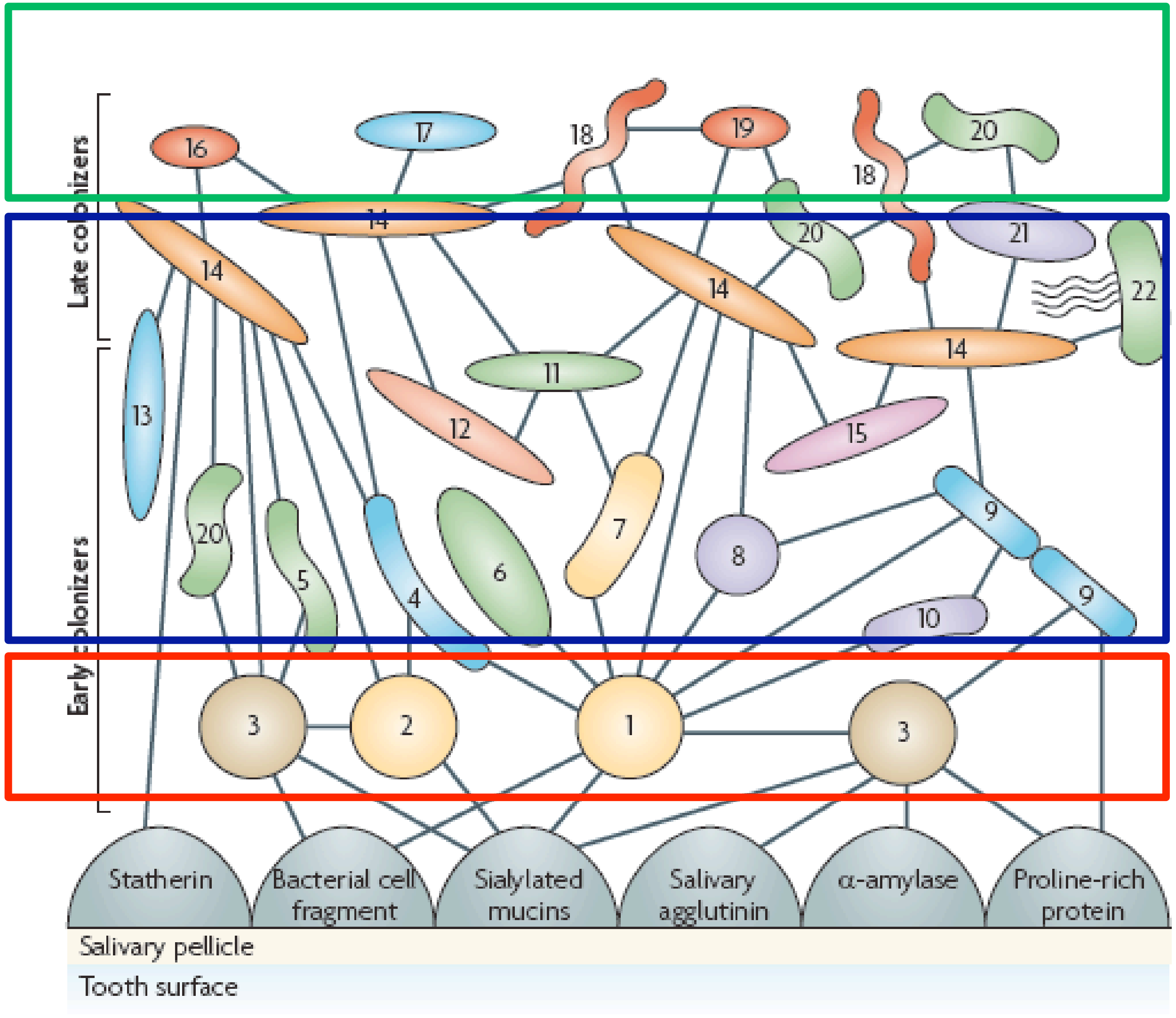
Day 1 1436 mm^2



Day 10 22,522 mm^2



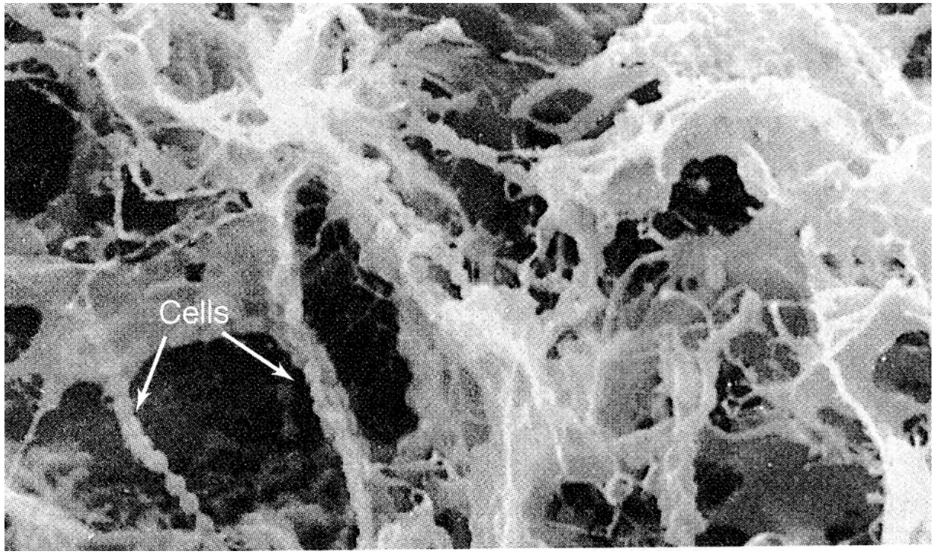
Microbiota of the Dental plaques: The Colonizers' Pyramid

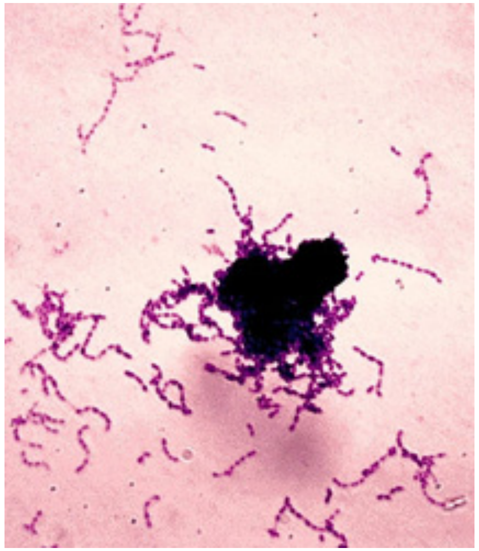


1. *Streptococcus oralis* and *Streptococcus sanguinis*
2. *Streptococcus mitis*
3. *Streptococcus gordonii*
4. *Capnocytophaga ochracea*
5. *Propionibacterium acnes*
6. *Haemophilus parainfluenzae*
7. *Prevotella loescheii*
8. *Veillonella* spp.
9. *Actinomyces oris* and *Actinomyces naeslundii*
10. *Eikenella corrodens*
11. *Actinomyces israelii*
12. *Capnocytophaga gingivalis*
13. *Capnocytophaga sputigena*
14. *Fusobacterium nucleatum*
15. *Prevotella denticola*
16. *Aggregatibacter actinomycetemcomitans*
17. *Eubacterium* spp.
18. *Treponema denticola*
19. *Tannerella forsythia*
20. *Porphyromonas gingivalis*
21. *Prevotella intermedia*
22. *Selenomonas flueggei*

Dental plaque: the first colonizers

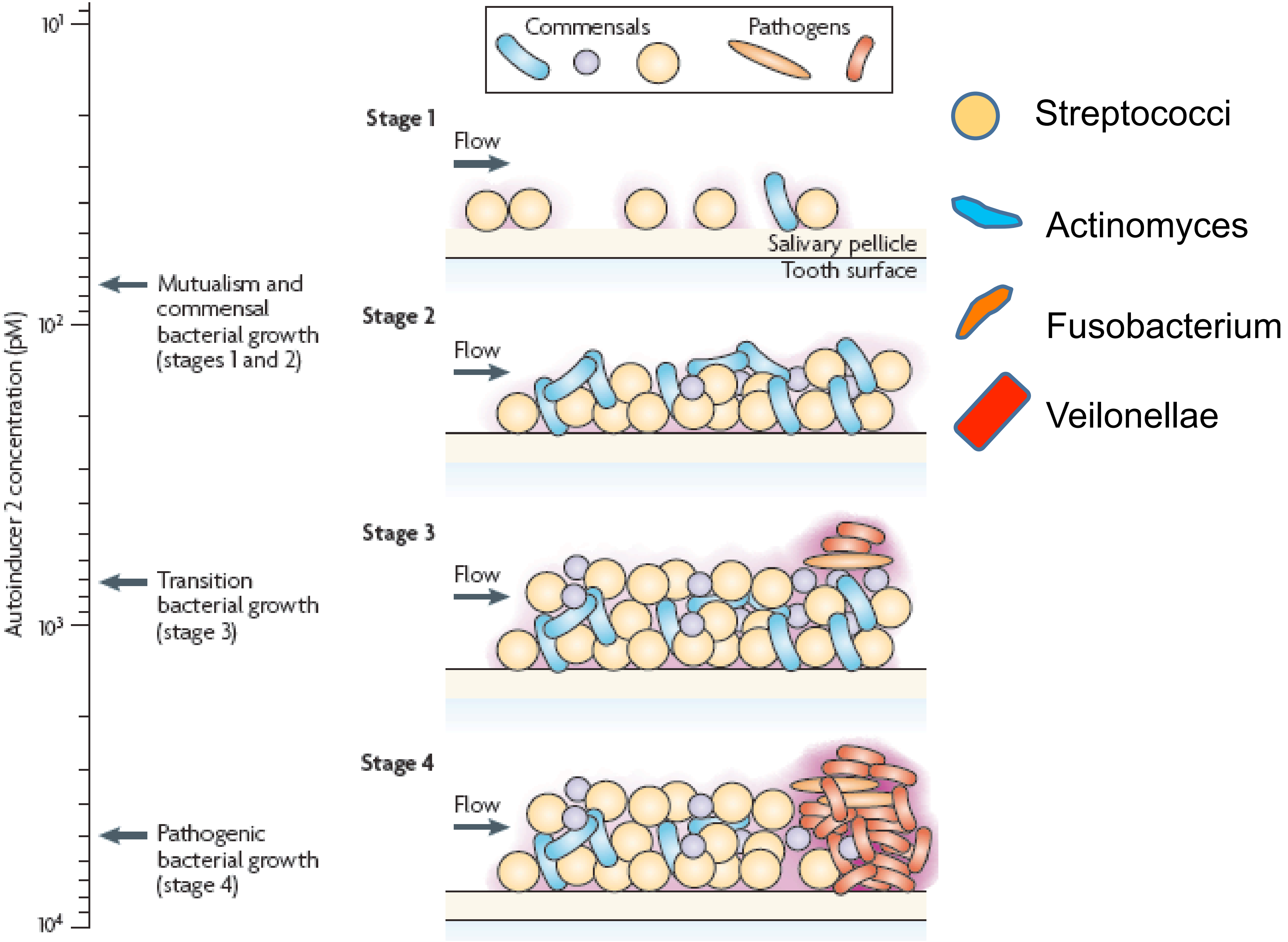
Streptococcus mutans, mitis, sobrinus, suis





$$n\text{Sucrose} \xrightarrow{\text{Dextransucrase}} \text{Dextran } (n\text{Glucose}) + n\text{Fructose}$$

Development of dental plaques and quorum sensing



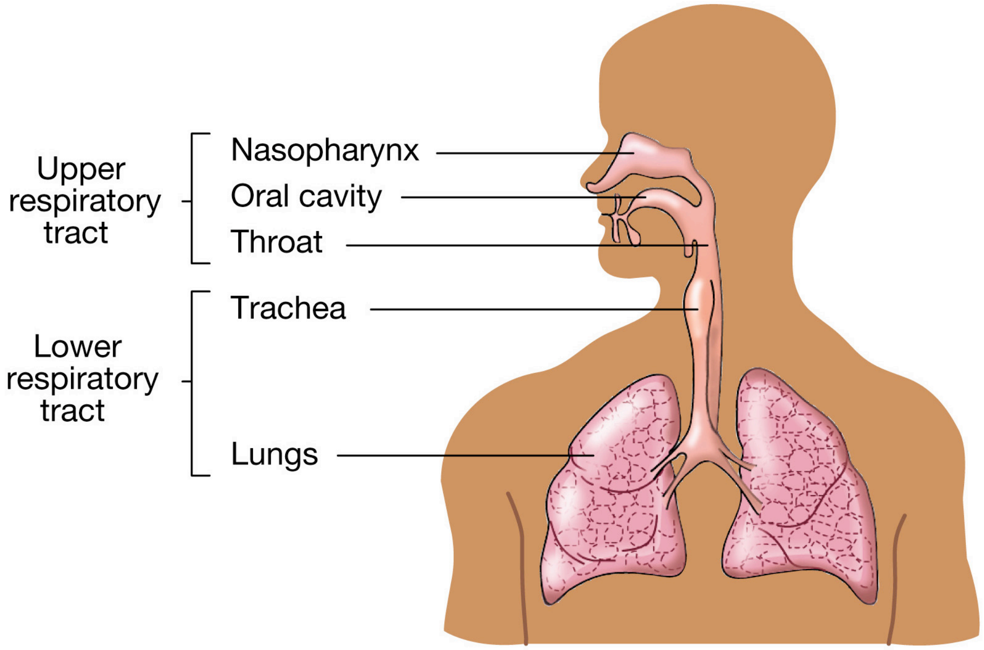
Streptococci

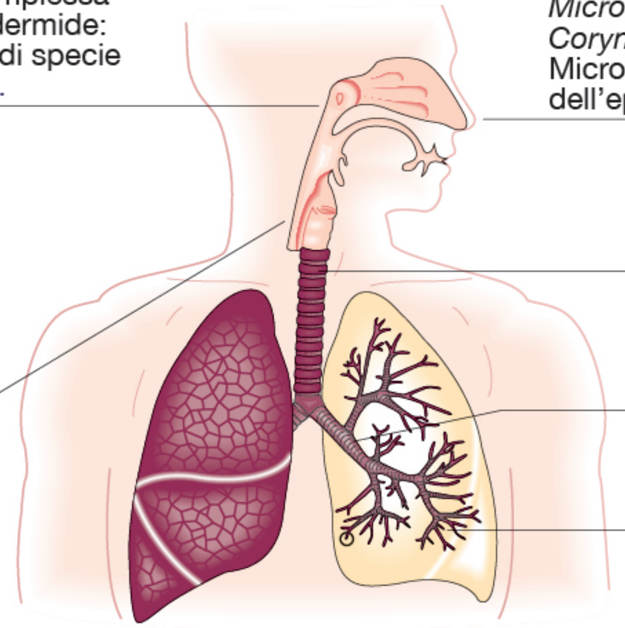
Actinomyces

Fusobacterium

Veilonellae

Microbiota of the respiratory tract





Naso-faringe
(*Staphylococcus* spp.,
Micrococcus spp.,
Corynebacterium spp.,
Neisseria spp.,
Haemophilus spp.).
Microflora più complessa
di quella dell'epidermide:
maggior numero di specie
causano malattie.

Narice anteriore
(*Staphylococcus* spp.,
Micrococcus spp.,
Corynebacterium spp.).
Microflora simile a quella
dell'epidermide

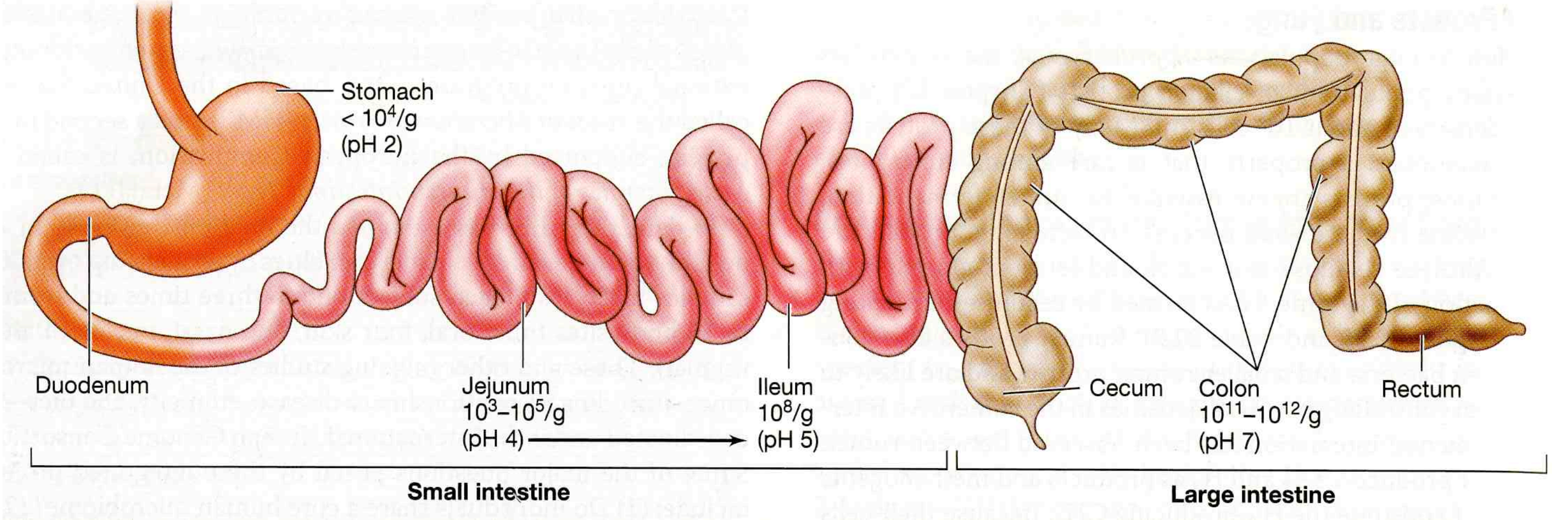
Orofaringe
Microflora differente
da quella del naso-faringe,
complessa e contenente
specie potenzialmente
patogene, quali *S. pyogenes*,
S. pneumoniae.

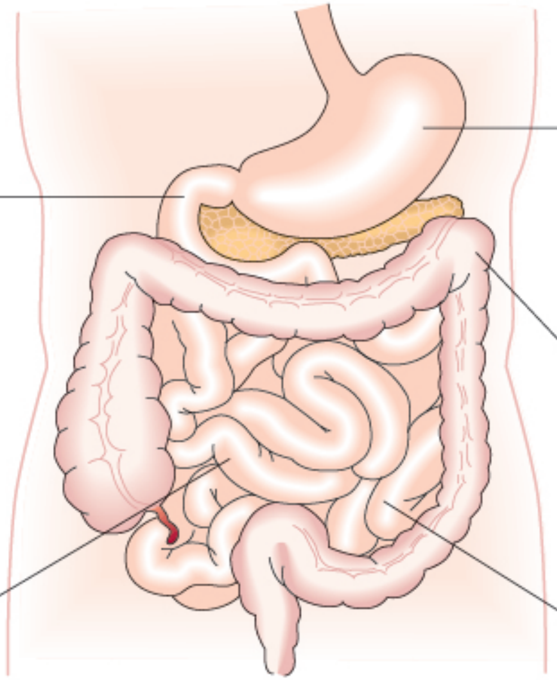
Trachea
(Normalmente sterile)

Bronchi
(Normalmente sterili)

Alveoli
(Normalmente sterili)

Microbiota of the human gastrointestinal tract





Duodeno
(scarsamente popolato; microflora più complessa dello stomaco; predominanza di streptococchi, lattobacilli, *Bacteroides* spp., *Bifidobacterium* spp.)

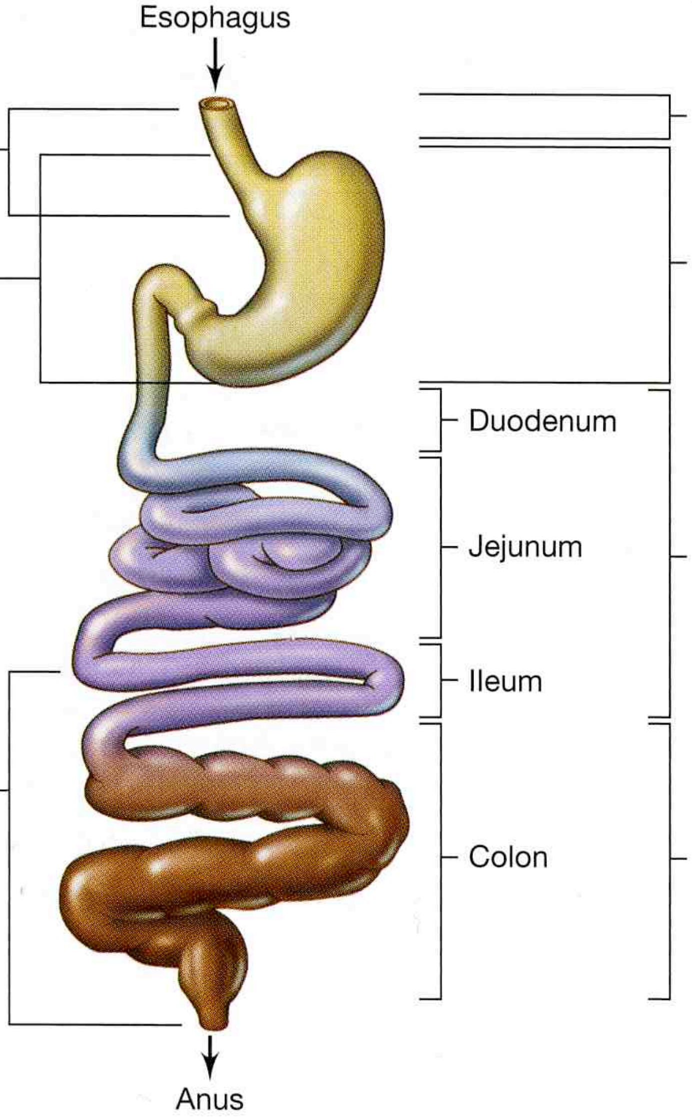
Digiuno
(scarsamente popolato; microflora più complessa dello stomaco; predominanza di streptococchi, lattobacilli, *Bacteroides* spp., *Bifidobacterium* spp.)

Stomaco
(scarsamente popolato; predominanza di streptococchi e lattobacilli; frequente presenza di *Helicobacter pylori*)

Colon
(molto densamente popolato; microflora molto complessa; predominio di anaerobi obbligati)

Ileo
(più densamente popolato del digiuno; microflora complessa)

Microbiota of the human gastrointestinal tract



Major bacteria present

Prevotella
Streptococcus
Veillonella

Helicobacter
Proteobacteria
Bacteroidetes
Actinobacteria
Fusobacteria

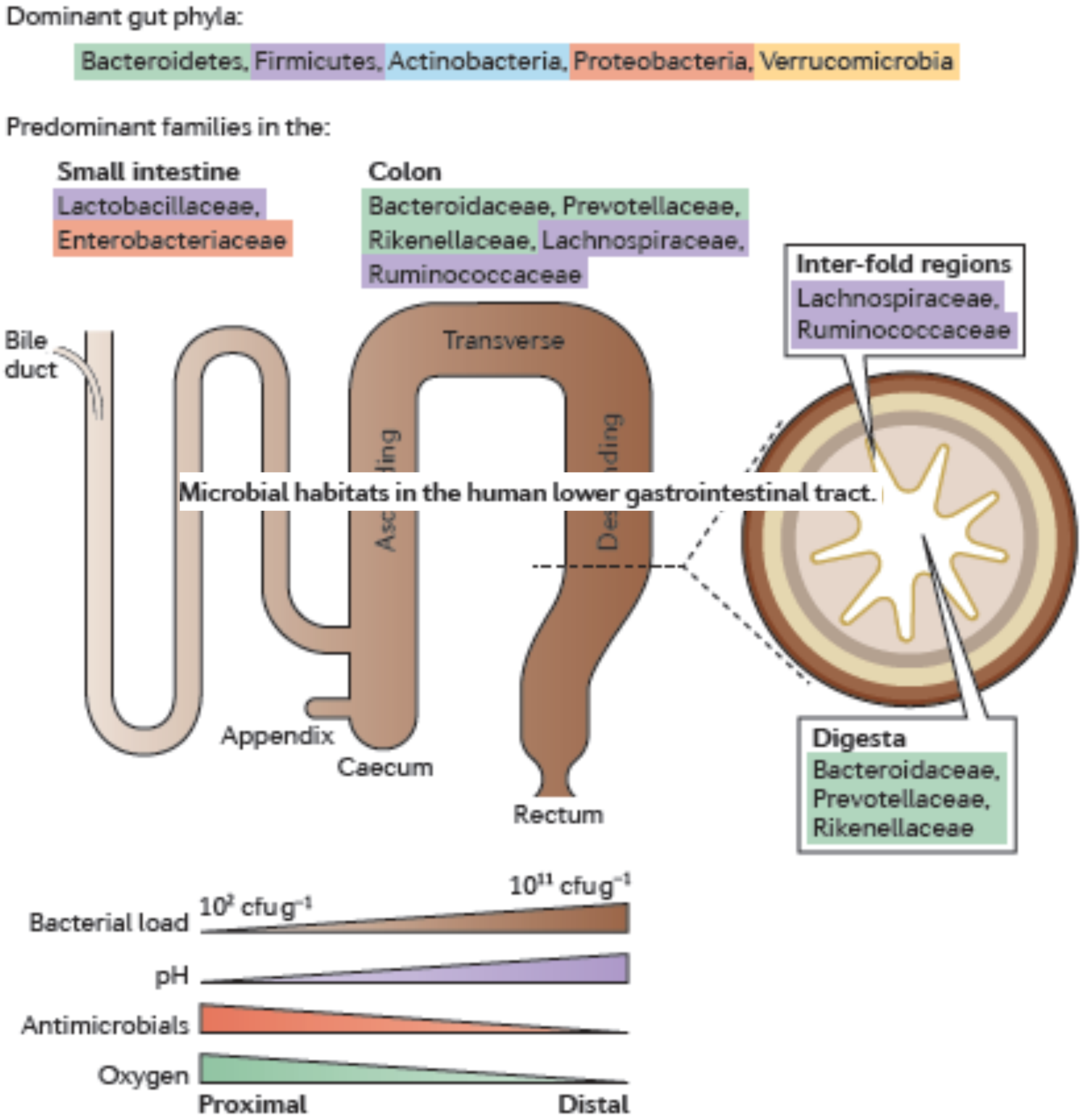
Enterococci
Lactobacilli

Bacteroides
Bifidobacterium
Clostridium
Enterobacteria
Enterococcus
Escherichia
Eubacterium
Klebsiella
Lactobacillus
Methanobrevibacter *(Archaea)*
Peptococcus
Peptostreptococcus
Proteus
Ruminococcus
Staphylococcus
Streptococcus

Organ	**Major physiological processes**
Esophagus	
Stomach	Secretion of acid (HCl) Digestion of macromolecules **pH 2**
Small intestine	Continued digestion Absorption of monosaccharides, amino acids, fatty acids, water **pH 4–5**
Large intestine	Absorption of bile acids, vitamin B_{12} **pH 7**

Microorgansim	Range of Incidence
Bacteroides fragilis	100
Bacteroides melaninogenicus	100
Bacteroides oralis	100
Lactobacillus	20-60
Clostridium perfringens	25-35
Clostridium septicum	5-25
Clostridium tetani	1-35
Bifidobacterium bifidum	30-70
Staphylococcus aureus	30-50
Enterococcus faecalis	100
Escherichia coli	100
Salmonella enteritidis	3-7
Salmonella typhi	0.00001
Klebsiella sp.	40-80
Enterobacter sp.	40-80
Proteus mirabilis	5-55
Pseudomonas aeruginosa	3-11
Peptostreptococcus sp.	common
Peptococcus sp.	moderate
Methanogens (Archaea)	common

Microbial habitats in the human lower gastrointestinal tract



Dominant gut phyla:

Bacteroidetes, Firmicutes, Actinobacteria, Proteobacteria, Verrucomicrobia

Predominant families in the:

Small intestine
Lactobacillaceae,
Enterobacteriaceae

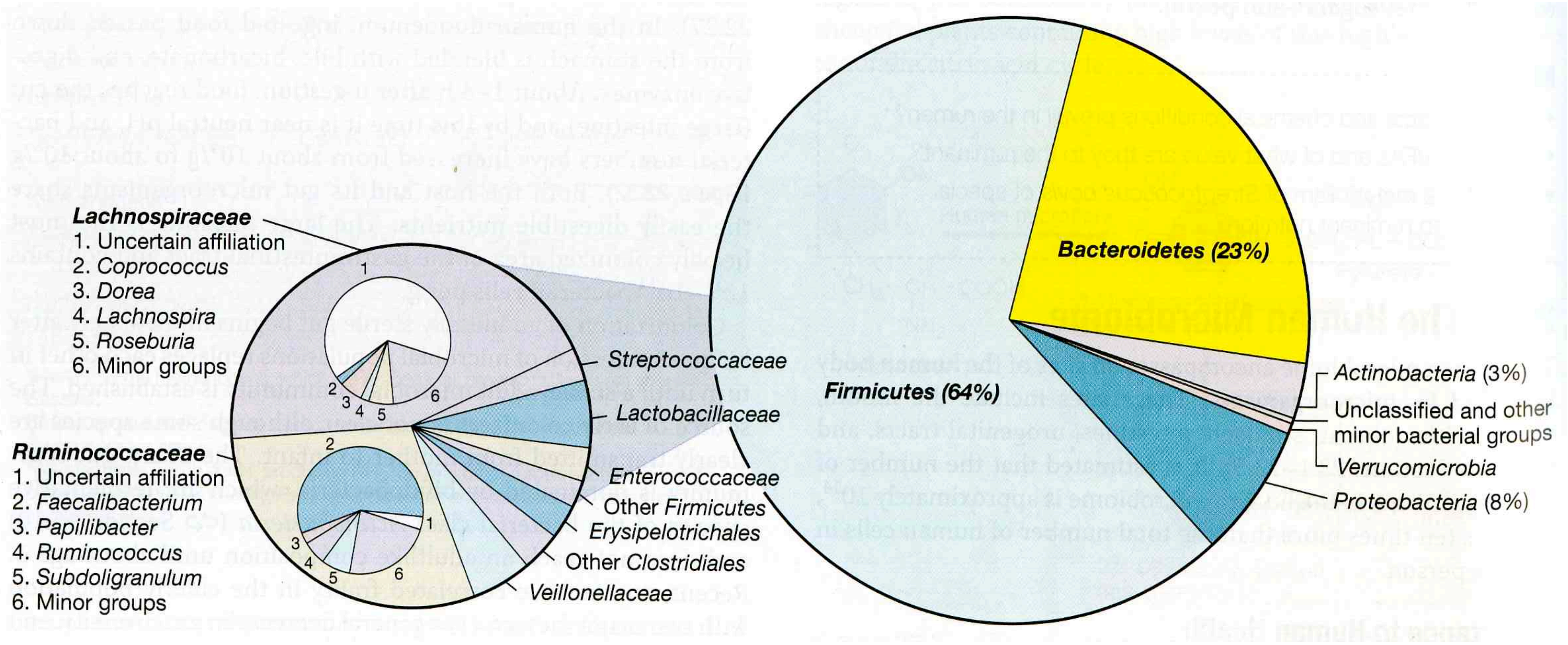
Colon
Bacteroidaceae, Prevotellaceae,
Rikenellaceae, Lachnospiraceae,
Ruminococcaceae

Inter-fold regions
Lachnospiraceae,
Ruminococcaceae

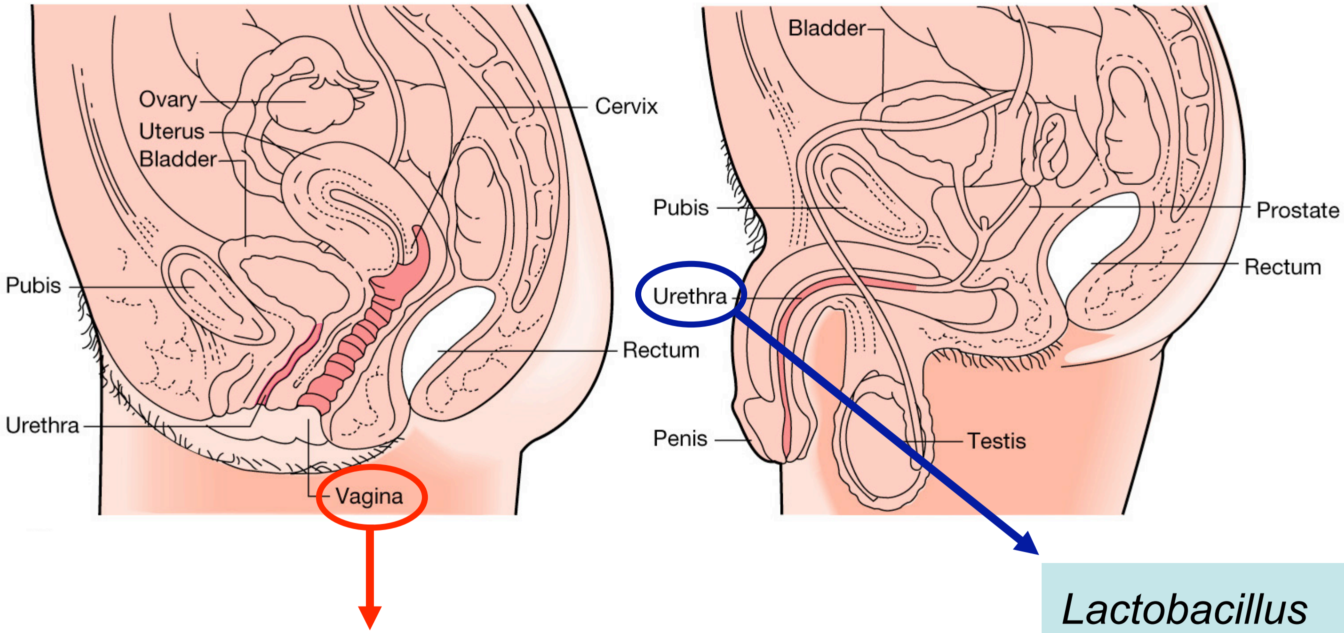
Digesta
Bacteroidaceae,
Prevotellaceae,
Rikenellaceae

Microbial habitats in the human lower gastrointestinal tract.

Microbial composition of the human colon inferred From 16S RRNA gene sequences



Microbiota of the urogenital tract



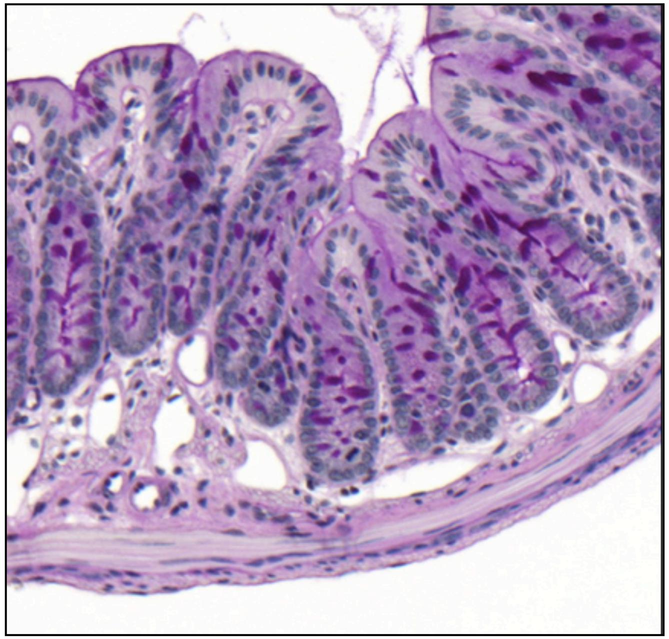
Lactobacillus
Streptococcus
Stafilococcus coag neg

Normal vaginal flora depends on hormonal levels of the host:

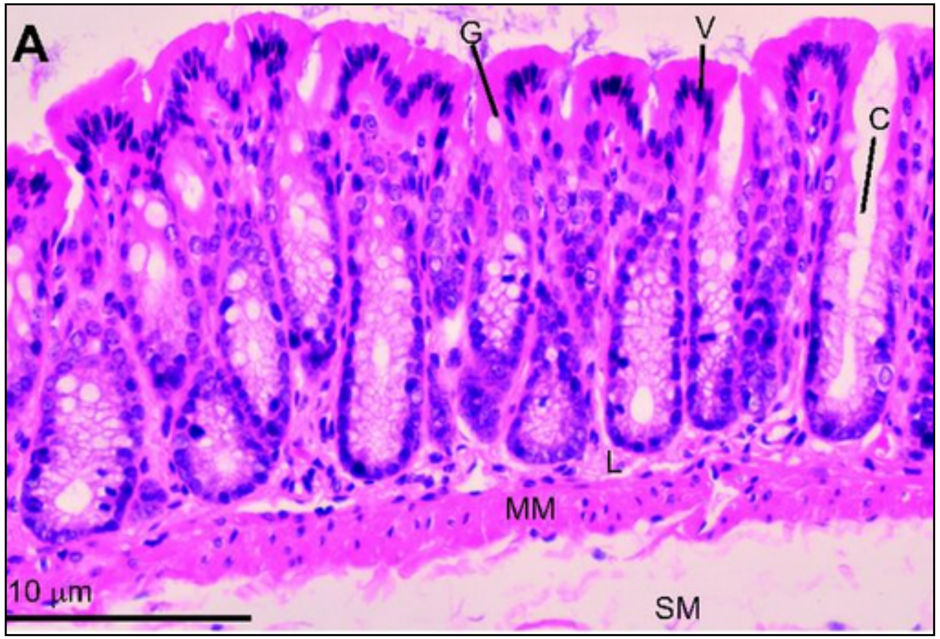
- **newborns:** *Lactobacillus*
- **infants:** *Stafilococcus, Streptococcus, Enterobacteriaceae*
- **from puberty:** *Lactobacillus, Stafilococcus, Streptococcus, Enterococcus, Enterobacteriaceae,anaerobic bacteria*
- **after menopause:** similar to that before puberty

Germ-free mice: role of the microbiota

Germ-free hosts, especially murine (rat or mouse) animals have become a powerful tool for exploring the interplay between the host and microorganisms inhabiting the human intestine



Gut from a germ-free mous



Gut from a wt mouse

Benefit of the normal human microbiota

- ✓ The normal flora synthesize and excrete vitamins (ex. enteric bacteria secrete Vitamin K and Vitamin B12).

- ✓ The normal flora prevent colonization by pathogens competing for attachment sites or for essential nutrients.

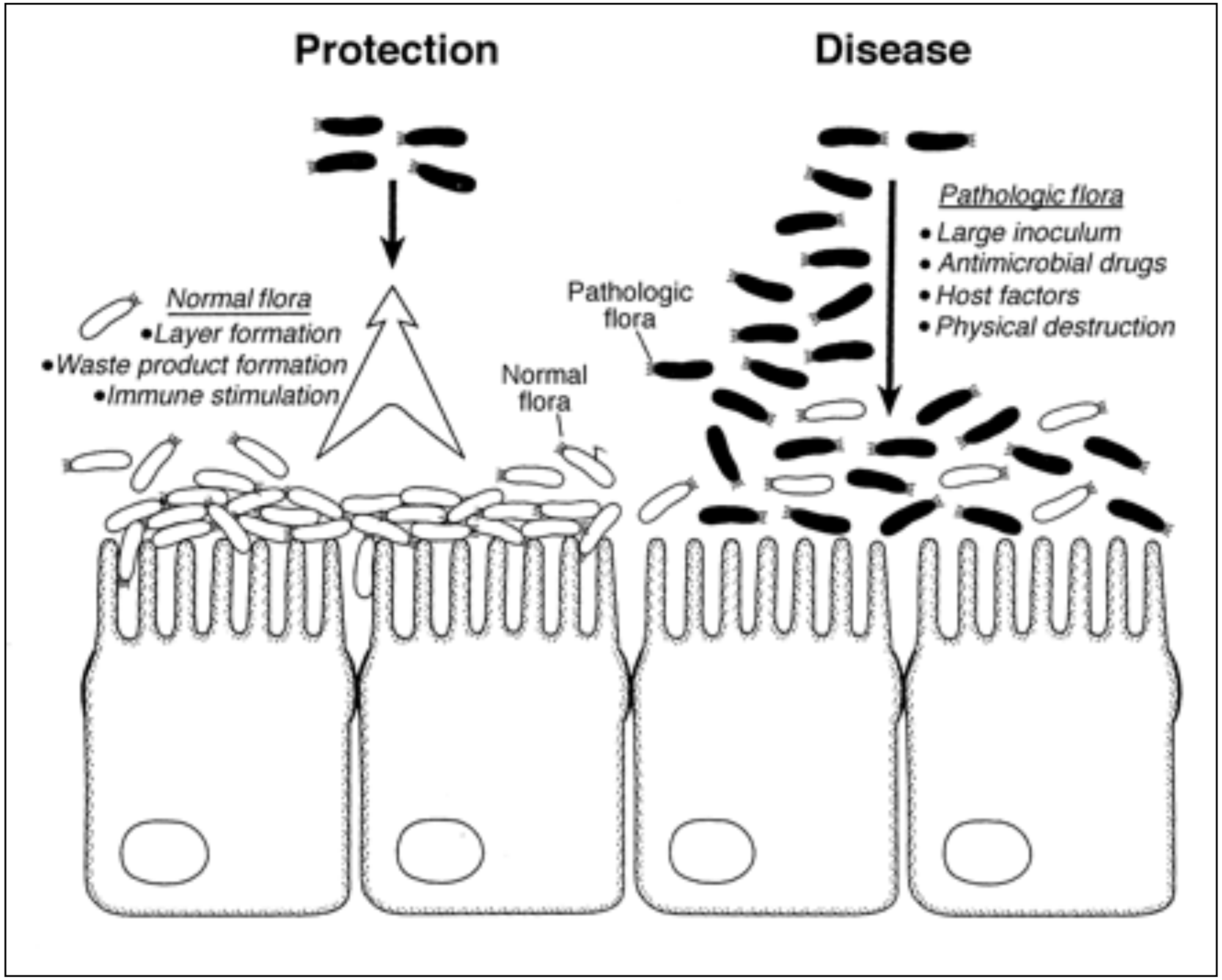
- ✓ The normal flora may antagonize other bacteria through the production of substances which inhibit or kill nonindigenous species (ex. bacteriocins).

- ✓ The normal flora stimulate the development of certain tissues (ex. the caecum and certain lymphatic tissues in the GI tract).

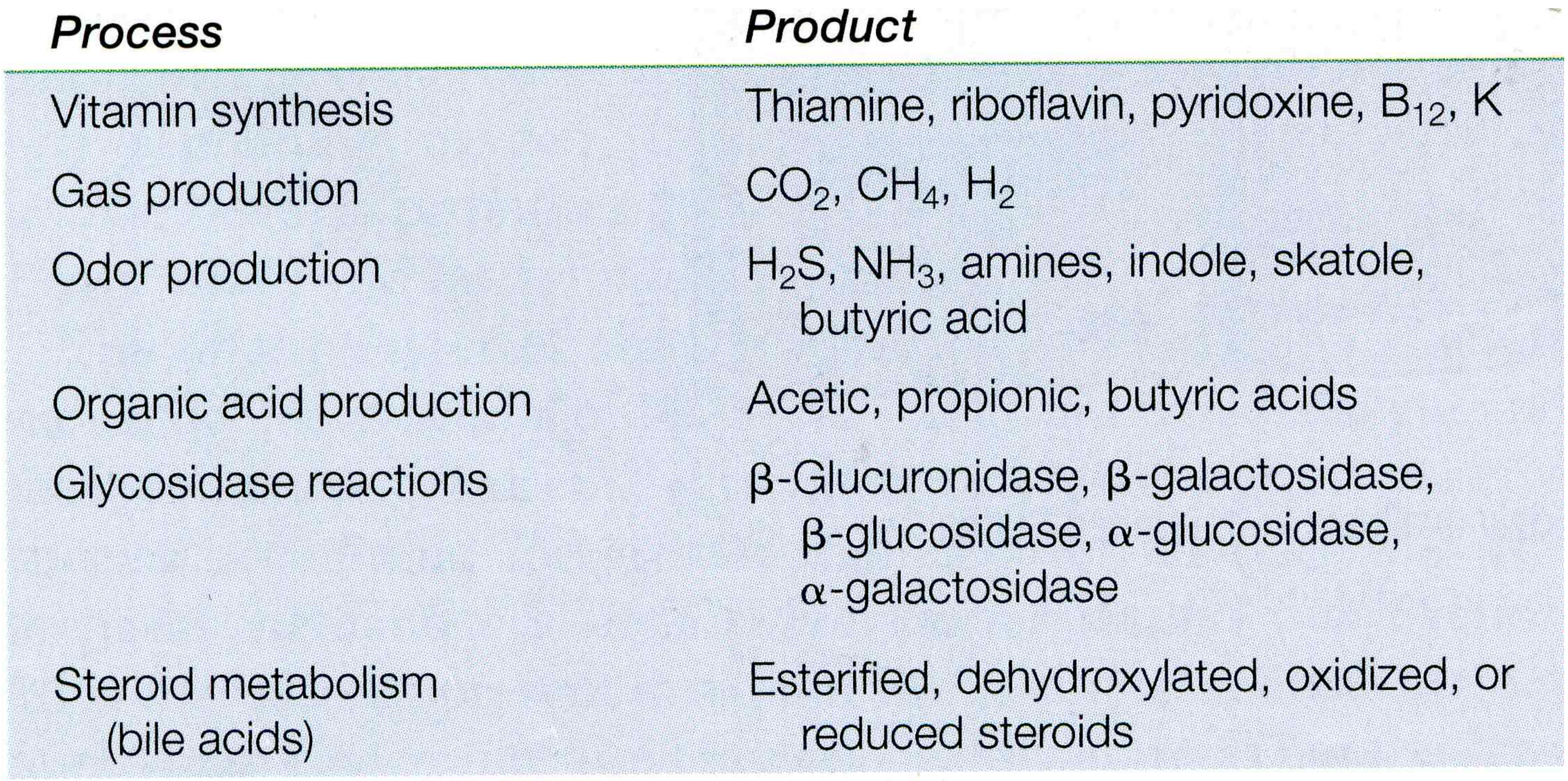
- ✓ The normal flora stimulate the production of cross-reactive antibodies

Benefit of the normal human microbiota

Mechanisms by which the normal flora competes with invading pathogens:
the surface exclusion

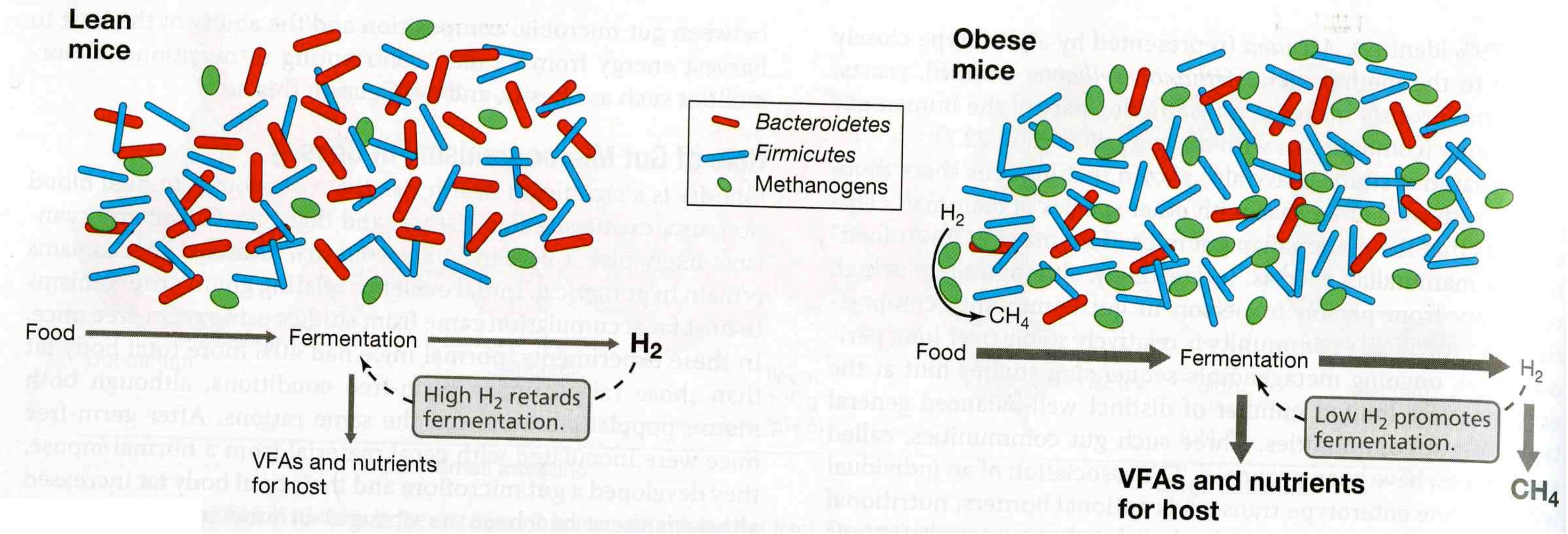


Biochemical/metabolic contribution of intestinal microorganisms

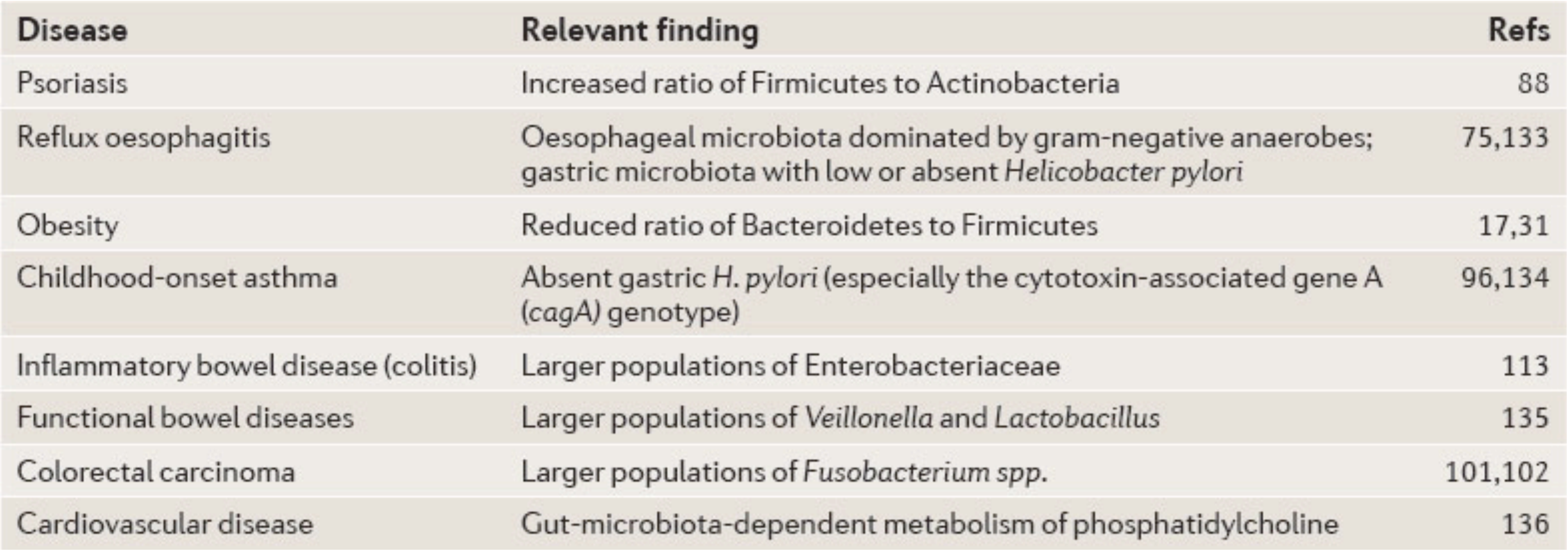


Process	***Product***
Vitamin synthesis	Thiamine, riboflavin, pyridoxine, B_{12}, K
Gas production	CO_2, CH_4, H_2
Odor production	H_2S, NH_3, amines, indole, skatole, butyric acid
Organic acid production	Acetic, propionic, butyric acids
Glycosidase reactions	β-Glucuronidase, β-galactosidase, β-glucosidase,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

Differences in the gut microbial communities between lean and obese mice



Examples of associations of human conditions with particular microbiota characteristics



Disease	Relevant finding	Refs
Psoriasis	Increased ratio of Firmicutes to Actinobacteria	88
Reflux oesophagitis	Oesophageal microbiota dominated by gram-negative anaerobes; gastric microbiota with low or absent *Helicobacter pylori*	75,133
Obesity	Reduced ratio of Bacteroidetes to Firmicutes	17,31
Childhood-onset asthma	Absent gastric *H. pylori* (especially the cytotoxin-associated gene A (*cagA*) genotype)	96,134
Inflammatory bowel disease (colitis)	Larger populations of Enterobacteriaceae	113
Functional bowel diseases	Larger populations of *Veillonella* and *Lactobacillus*	135
Colorectal carcinoma	Larger populations of *Fusobacterium spp.*	101,102
Cardiovascular disease	Gut-microbiota-dependent metabolism of phosphatidylcholine	136