Introduction to Microbiology

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Human microbiota

Microbiota

- Throughout thousands of years, humans of various origins and lifestyles collected a **unique array of non-pathogenic microorganisms**, Mostly **bacteria**, and recently recognized fungi and even viruses.

- This microbiota is established **early in life** and changes throughout life. Some are considered **resident** and some are **transient**.

- Almost **1.3:1 bacteria:human cell number**. Previously said to be 10:1.

- Not all bacteria are bad, some are even beneficial.

- Each organ has its unique microbiota.

- Studying and characterizing our microbiota is a burgeoning field of research !

Microbiota

- A **microbiota** is an "ecological community of commensal, symbiotic and pathogenic microorganisms" found in and on all multicellular organisms studied to date from plants to animals.

- The synonymous term **microbiome** describes either the **collective genomes** of the microorganisms that reside in an environmental niche or the microorganisms themselves.

- Where is the human microbiota primarily found in the body?

- a) Only on the skin surface
- b) Exclusively in the gastrointestinal tract
- c) Distributed across various body sites such as the skin, oral cavity, gastrointestinal tract, and more
- d) Mainly in the respiratory system

The human microbiome project

In a broad attempt to understand the role played by resident microbial ecosystems in human health and disease, in **2007, the National Institutes of Health** launched the Human Microbiome Project. One of the main goals of this project is **to understand the range of human genetic and physiologic diversity of** the microbiome, and the factors that influence the distribution and evolution of the constituent microorganisms.

Microbial communities will be investigated using **small-subunit (16S) ribosomal RNA gene sequencing.** Other tools could include **Mass spectrometry. Culturing could be difficult** and would under represent the variation since not all microbes are culturable.

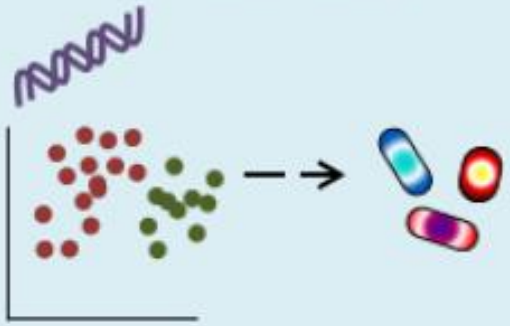
How stable and resilient is an individual's microbiota throughout one day and during his or her lifespan? **How similar** are the microbiomes between members of a family or members of a community or across communities in different environments?
Do all humans have an identifiable "core" microbiome, and if so, how is it **acquired and transmitted**? What affects the genetic diversity of the microbiome, and how does this diversity affect adaptation by the microorganisms and the host to markedly **different lifestyles and to various physiological or pathophysiological states**?

The human microbiome project

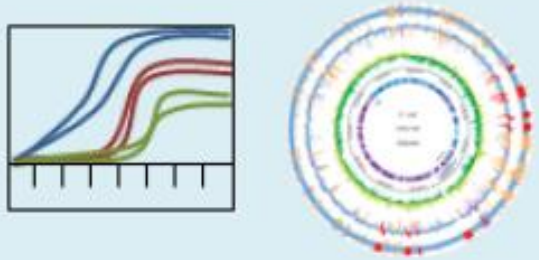
DNA-Based Approaches

Who is there?
What can they do?

16S rRNA, 18S, ITS gene sequencing



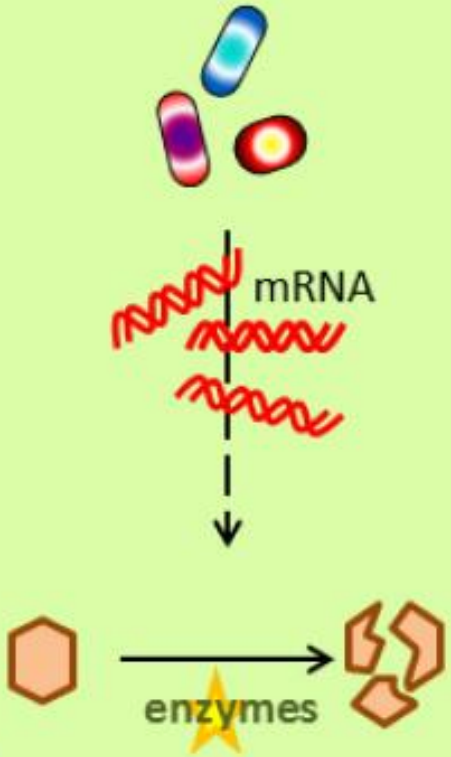
metagenomics



RNA-Based Approaches

How do they respond?
What pathways are activated?

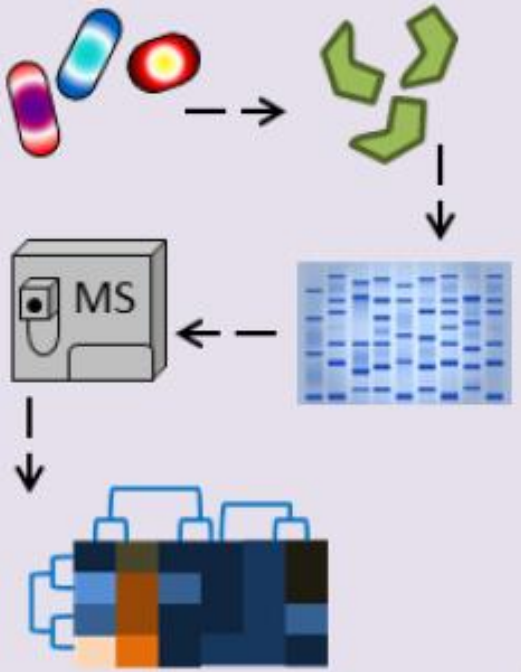
metatranscriptomics



Protein-Based Approaches

How are they interacting with the host?
What proteins are being produced?

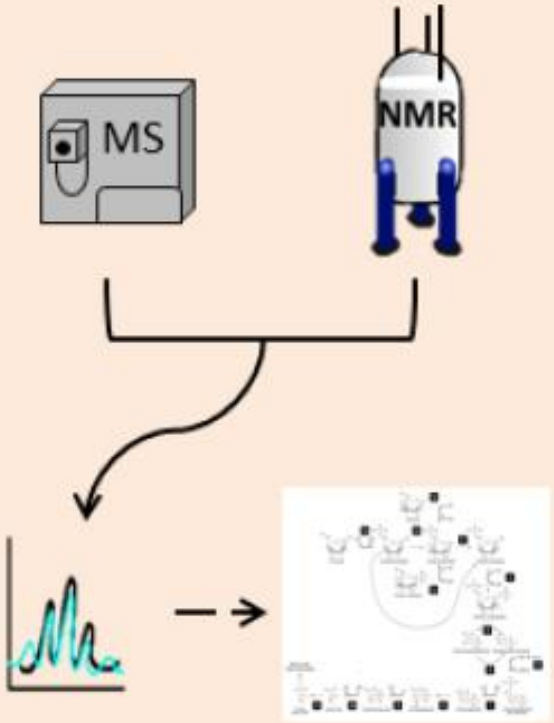
metaproteomics



Metabolite-Based Approaches

What are the chemical outcomes of their activity?

metabolomics



The most commonly used way to investigate the diversity of bacterial microbiota species in a sample from the human gut is:

A. Use of selective culture media
B. Use of differential culture media
C. Biochemical testing
D. DNA-based approaches (e.g. metagenomics)

The skin microbiota

Despite the harsh physical landscape of skin, **particularly the desiccated, nutrient-poor, acidic environment, fatty acids in sebaceous secretions, and the presence of lysozyme and antimicrobial peptides**, the skin is colonized by a diverse microbiota.

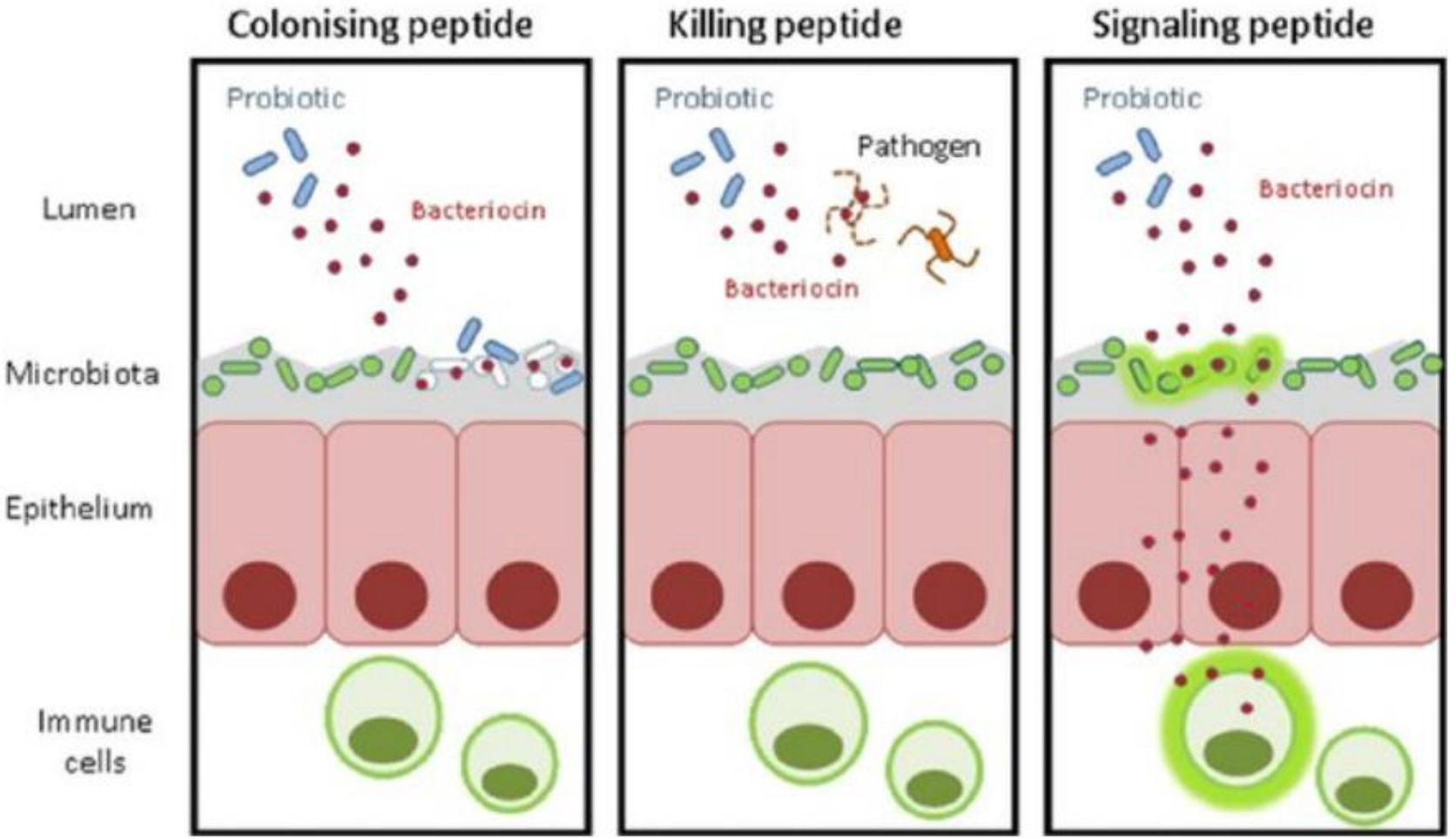
The skin is particularly apt to contain **transient microorganisms**. Nevertheless, there is a constant and well-defined resident flora, modified in different anatomic areas by **secretions, habitual wearing of clothing, or proximity to mucous membranes** (mouth, nose, and perineal areas.)

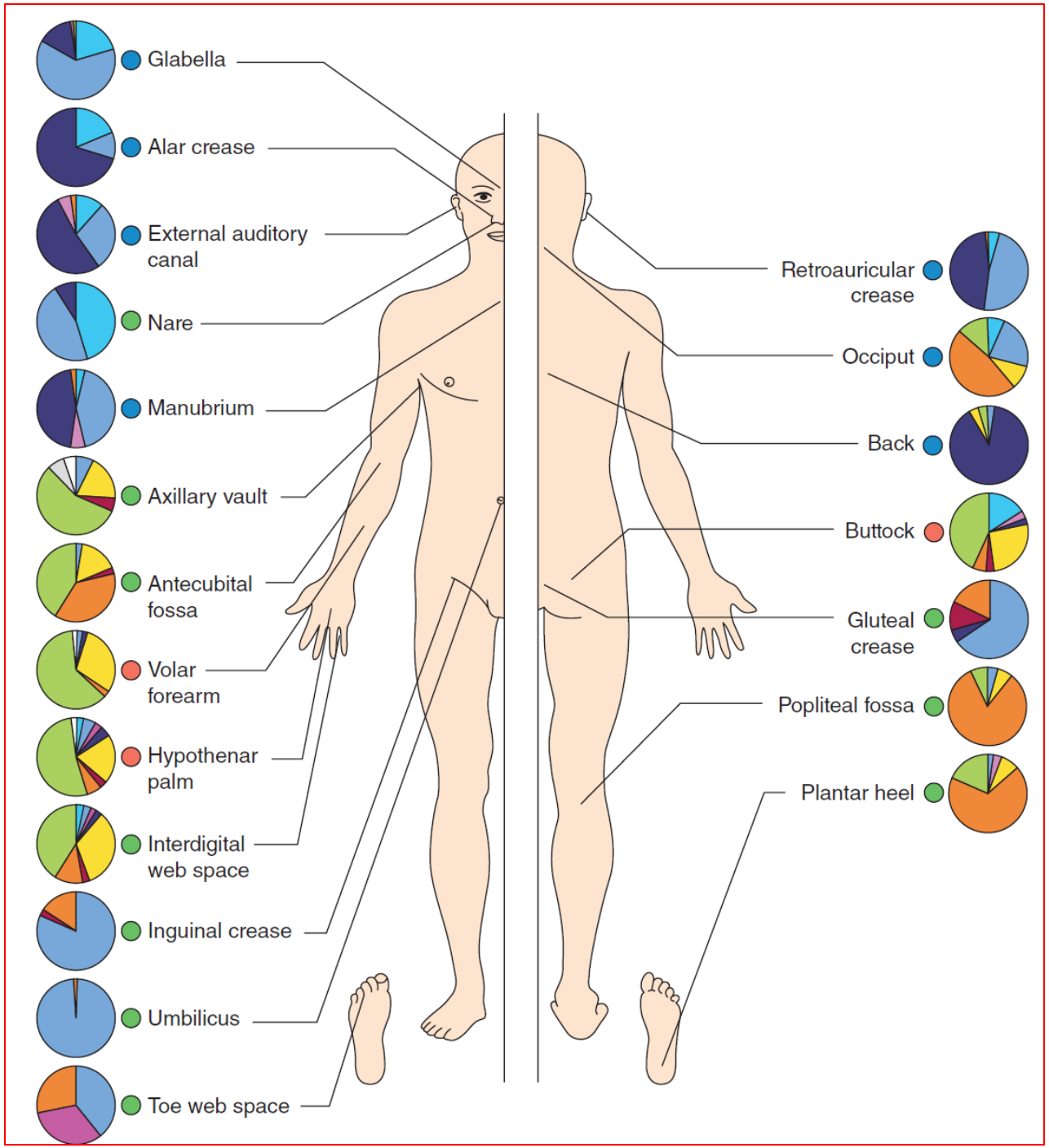
The predominant resident microorganisms of the skin are aerobic and anaerobic diphtheroid bacilli (eg, **Corynebacterium, Propionibacterium**); nonhemolytic aerobic and anaerobic staphylococci **(Staphylococcus epidermidis** and other **coagulase-negative staphylococci**).

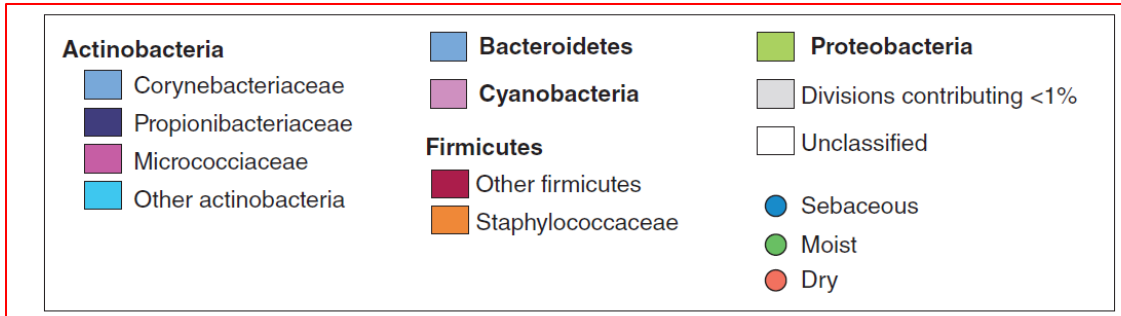
The skin microbiota is thought to help in fighting pathogenic bacteria, Disturbance of the skin barrier can lead to infections that might involve resident microbiota.

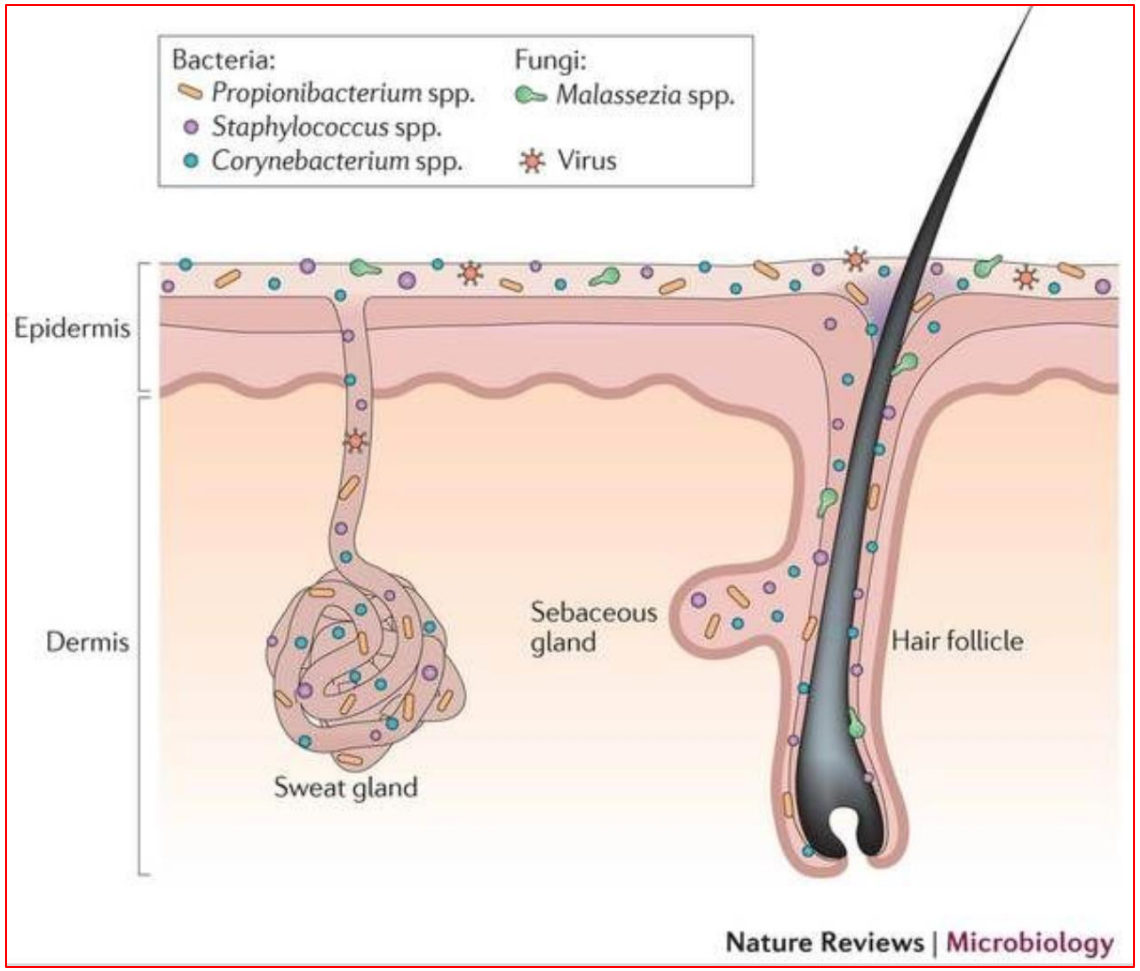
The skin microbiota

The commensal microbiota of the skin contributes to host health and is thought to play a role in protecting the host against a wide range of infections. One such defence mechanism is the production of bacteriocins.




Glabella
Alar crease
External auditory canal
Nare
Manubrium
Axillary vault
Antecubital fossa
Volar forearm
Hypothenar palm
Interdigital web space
Inguinal crease
Umbilicus
Toe web space
Retroauricular crease
Occiput
Back
Buttock
Gluteal crease
Popliteal fossa
Plantar heel


Actinobacteria
Corynebacteriaceae
Propionibacteriaceae
Micrococciaceae
Other actinobacteria
Bacteroidetes
Cyanobacteria
Firmicutes
Other firmicutes
Staphylococcaceae
Proteobacteria
Divisions contributing <1%
Unclassified
Sebaceous
Moist
Dry


Bacteria:
Propionibacterium spp.
Staphylococcus spp.
Corynebacterium spp.
Fungi:
Malassezia spp.
Virus
Epidermis
Dermis
Sebaceous gland
Hair follicle
Sweat gland
Nature Reviews | Microbiology

- The skin microbiota contributes to the body's immune system by:

- a) Triggering allergies
- b) Producing vitamin D
- c) Competing with potential pathogens
- d) Controlling blood sugar levels

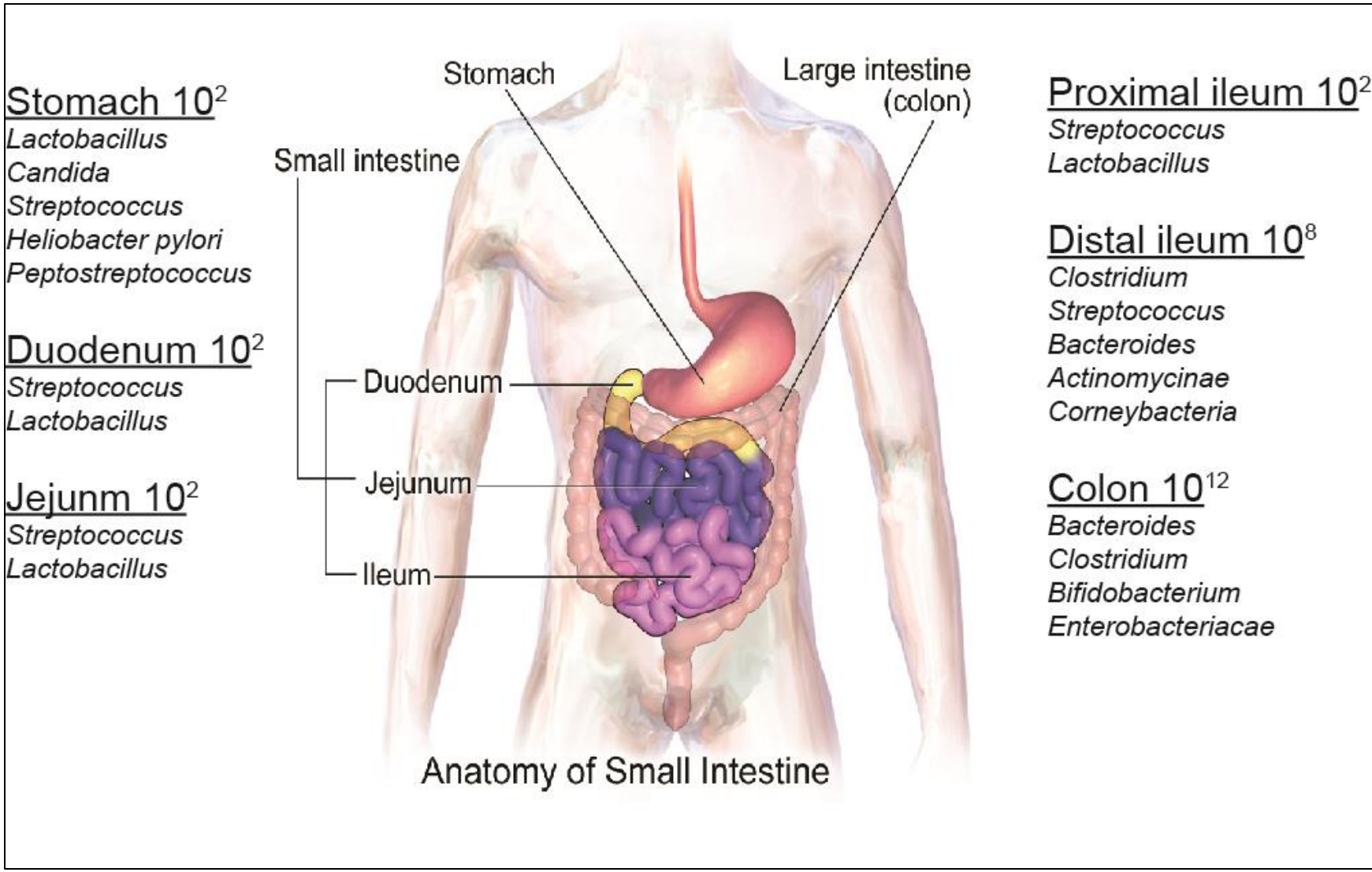
The gut microbiota

- Among the different non-sterile cavities, the human gut harbors the most complex microbiota, with a strong impact on host homeostasis and immunostasis, being thus essential for maintaining the health condition.

- The GIT microbiota exhibits a huge diversity, being individually shaped by numerous and incompletely elucidated factors, such as host **genetics**, **gender**, **age**, **immune system**, **health/disease condition**, **geographic** and socio-economical factors (urban or rural, sanitary conditions), **treatments**, **diet.**

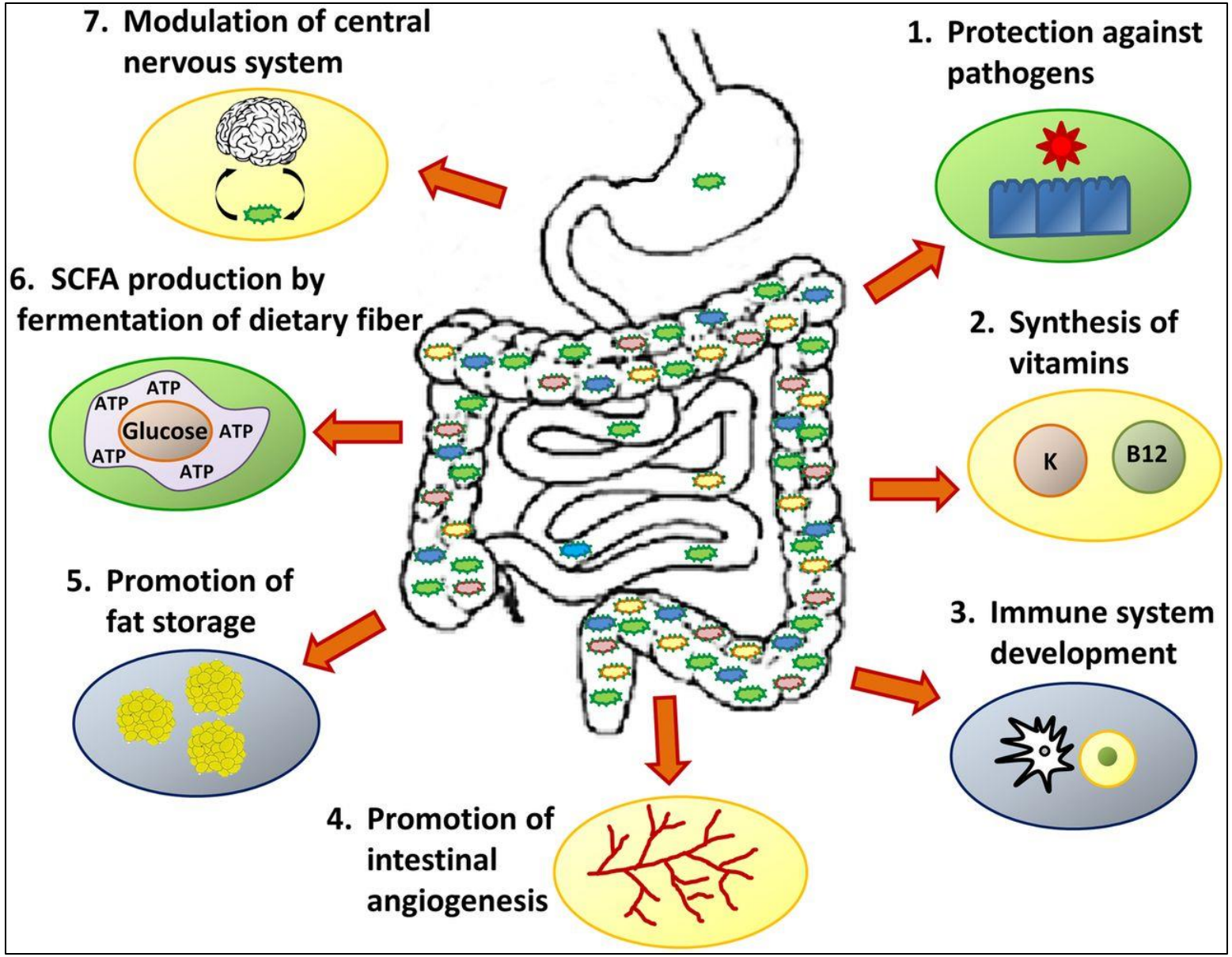
The gut microbiota

- The GIT contains at least 10^{14} microorganisms belonging to >1,000 species
- **Anaerobes outnumber facultative organisms in the colon by 1000-fold.**



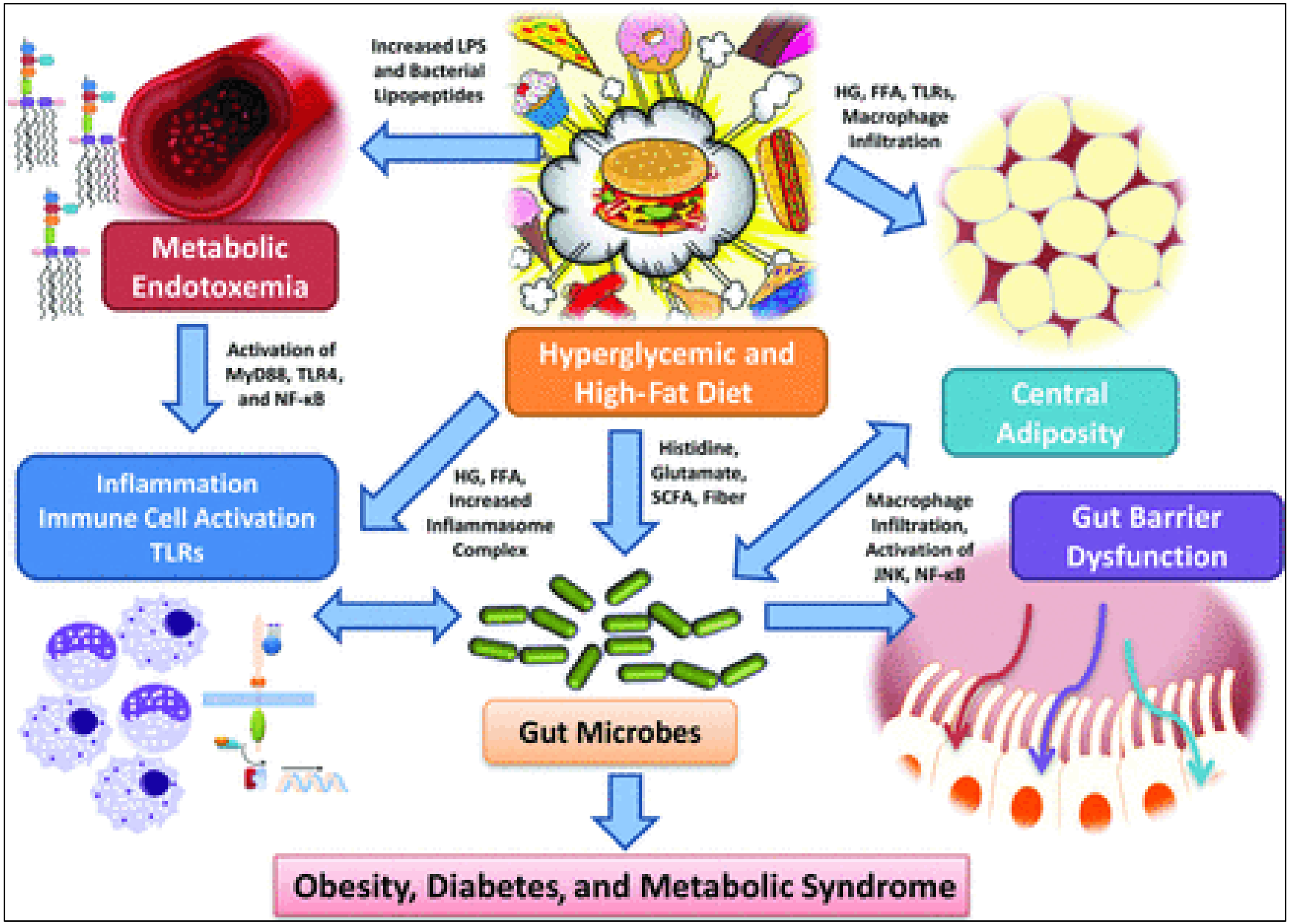
The gut microbiota

"Gut microbiota have beneficial effects offered to the host including providing essential nutrients by **metabolizing indigestible dietary compounds**, **defending against opportunistic pathogen colonization** by nutrient competition and **antimicrobial substance production**, and **contributing to intestinal epithelial barrier**. "



The gut microbiota

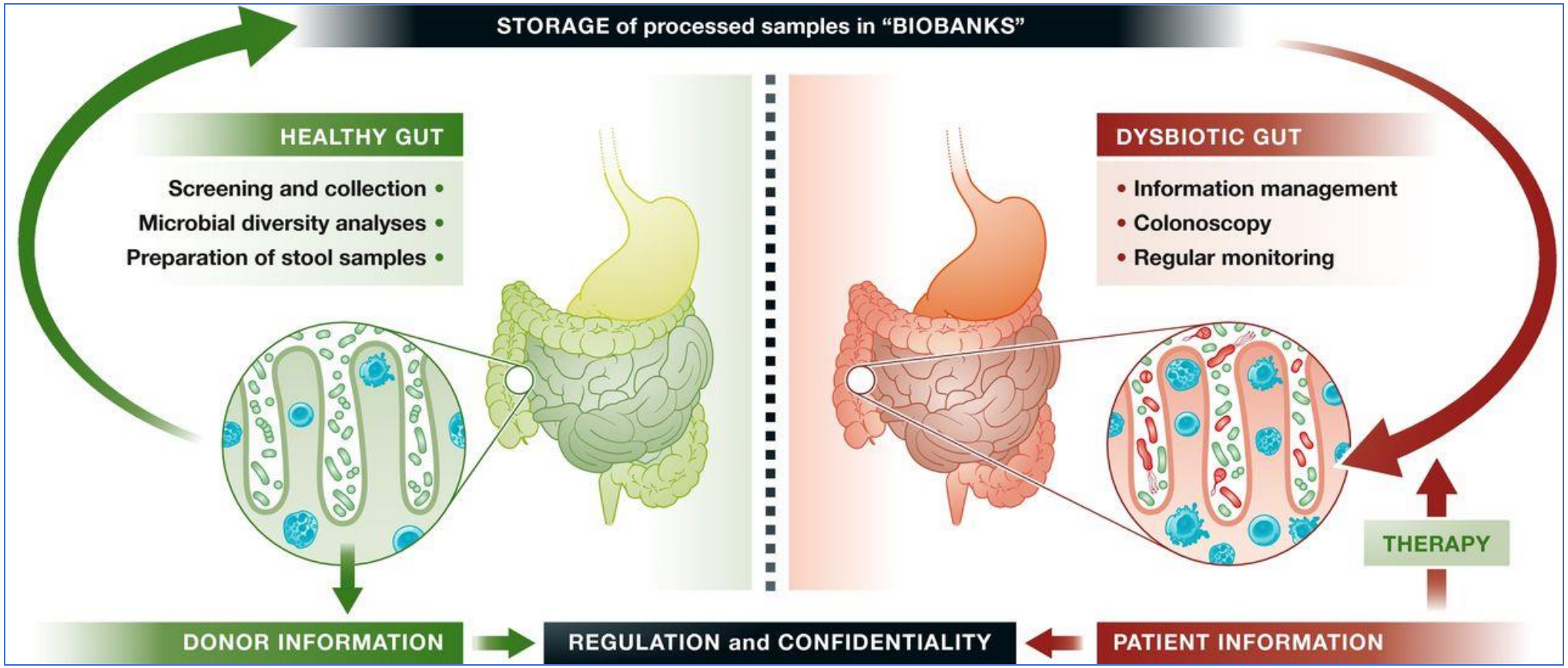
Food can affect the type of microbiome we have



The gut microbiota

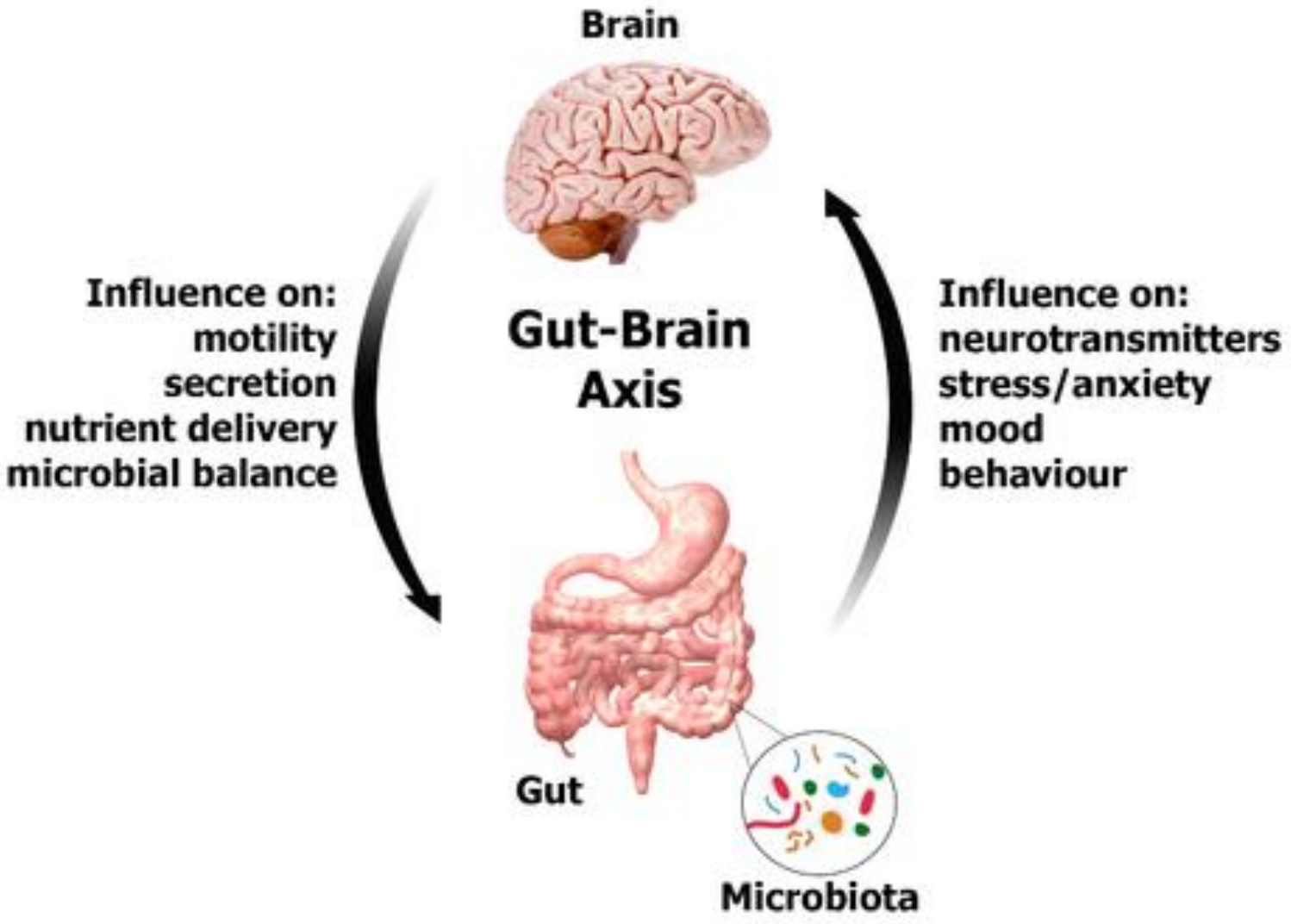
Effectiveness of **Fecal matter transplant** (FMT) has been established in clinical trials for the treatment of **Clostridium difficile** infection (CDI).

Future perspectives in microbiome studies involve finding the ”healthy” microbiome for individuals.



The gut microbiota

The altered bidirectional neurohumoral communication system between gut and brain – known as the gut-brain axis – may cause a series of diseases, such as autoimmune and CNS disorders



The respiratory tract microbiota

The microbiota of the respiratory tract probably acts as a gatekeeper that provides resistance to colonization by respiratory pathogens.

The respiratory microbiota might also be involved in the maturation and maintenance of respiratory physiology and immunity homeostasis.

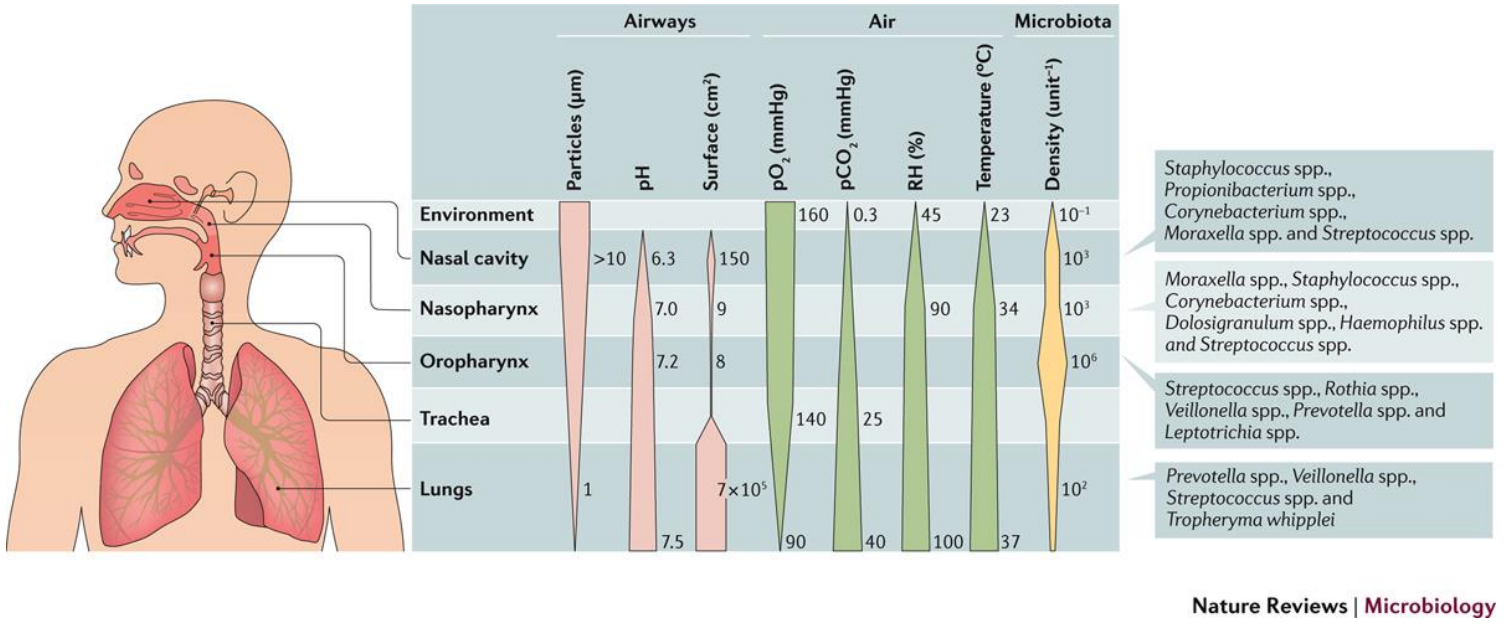
The pH gradually increases along the respiratory tract, whereas most of the increases in relative humidity (RH) and temperature occur in the nasal cavity, oxygen and carbon dioxide concentrations also vary along the respiratory tract.

inhalation results in the deposition of particles from the environment into the respiratory tract; inhaled particles that are more than 10 µm in diameter are deposited in the upper respiratory tract (URT), whereas particles less than 1 µm in diameter can reach the lungs. These particles include bacteria-containing and virus-containing particles, which are typically larger than 0.4 µm in diameter.

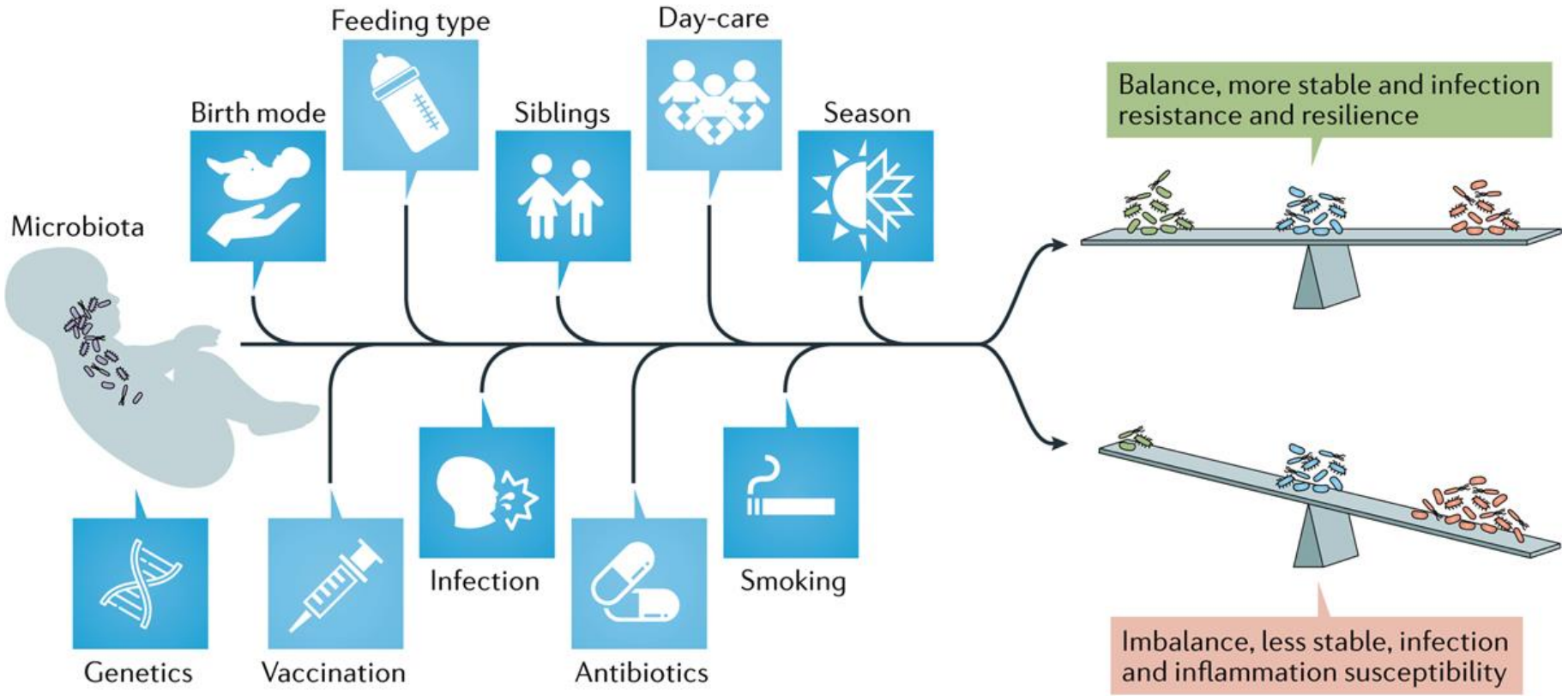
The respiratory tract microbiota

In healthy children and adults, a unique microbial community in the lungs was found that contained many of the bacteria that are common to the URT. A study in young children reported that although the lung microbiota was distinct from the microbiota of the URT, it was dominated by species that are also present in the URT, including Moraxella spp., Haemophilus spp., Staphylococcus spp. and Streptococcus spp.

In health, the lung microbiota is a community of **transiently present microorganisms** that are **derived from the URT**, rather than a thriving, resident community as is commonly found in chronic respiratory diseases.



The respiratory tract microbiota



The urogenital tract microbiota

The tip of the urethera can contain some bacteria that might appear in urine samples, yet emerging evidence indicates urine might not be sterile after all.

Soon after birth, **aerobic lactobacilli appear** in the vagina and persist as long as the pH remains acidic (several weeks). When the pH becomes neutral (remaining so until puberty), a mixed flora of cocci and bacilli is present. At puberty, aerobic and anaerobic **lactobacilli reappear** in large numbers and contribute to the maintenance of acid pH through the production of acid from carbohydrates.

Bacterial vaginosis is a syndrome marked by dramatic shifts in the types and relative proportions of the vaginal microbiota from a healthy environment containing Lactobacilli to a diseased one containing *Actinobacteria* and *Bacteroidetes* species.

Vaginally born infants have a microbiota containing species derived from the vaginal microbiota of their mothers. Conversely, in the case of cesarean section delivered babies, the microbiota is similar to the skin microbiota and is rich in Propionibacterium spp. and

The urogenital tract microbiota

Vaginally born infants **have a microbiota containing species derived from the vaginal microbiota of their mothers**. Conversely, in the case of **cesarean section** delivered babies, the microbiota is **similar to the skin microbiota** and is rich in Propionibacterium spp. and Staphylococcus spp.

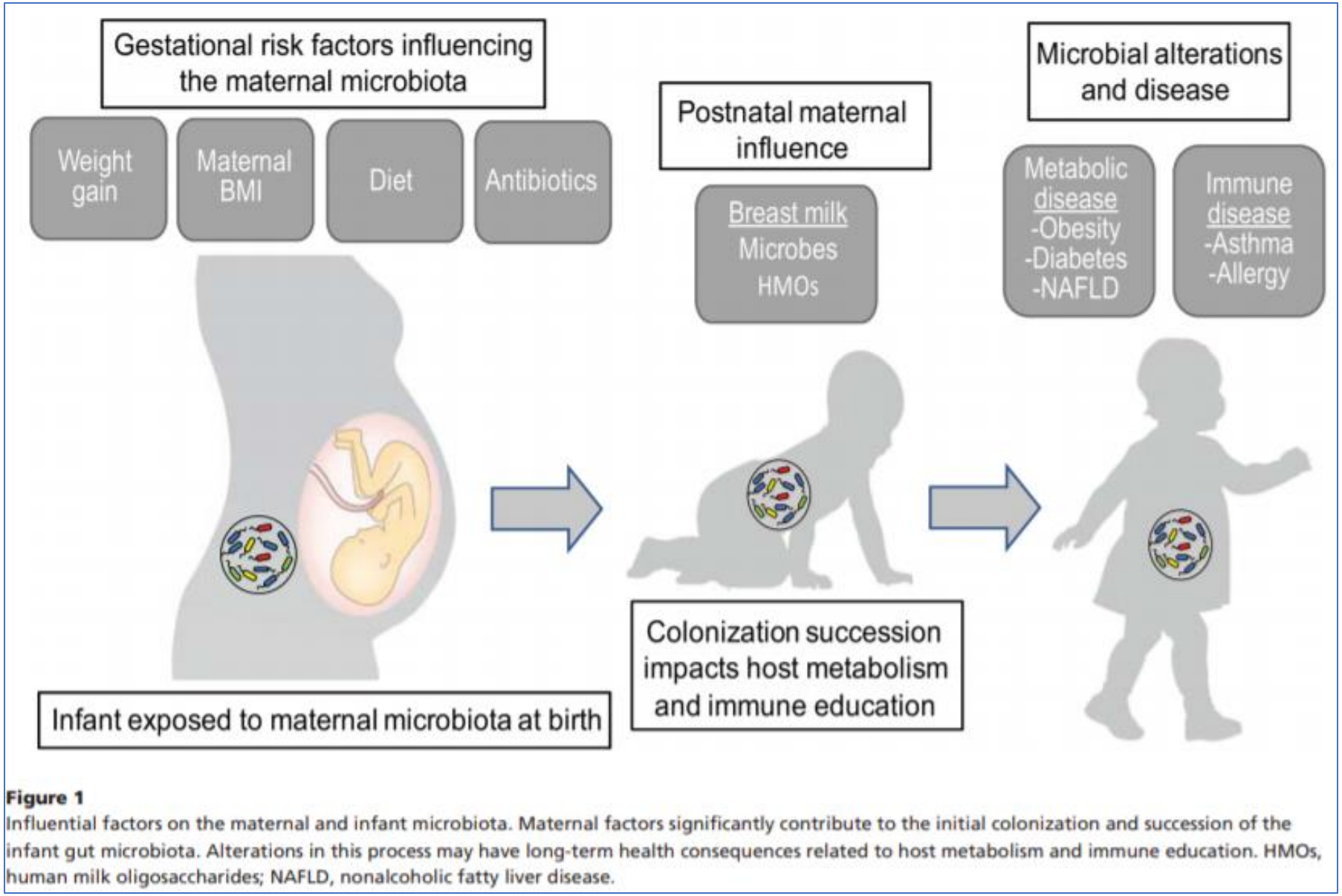
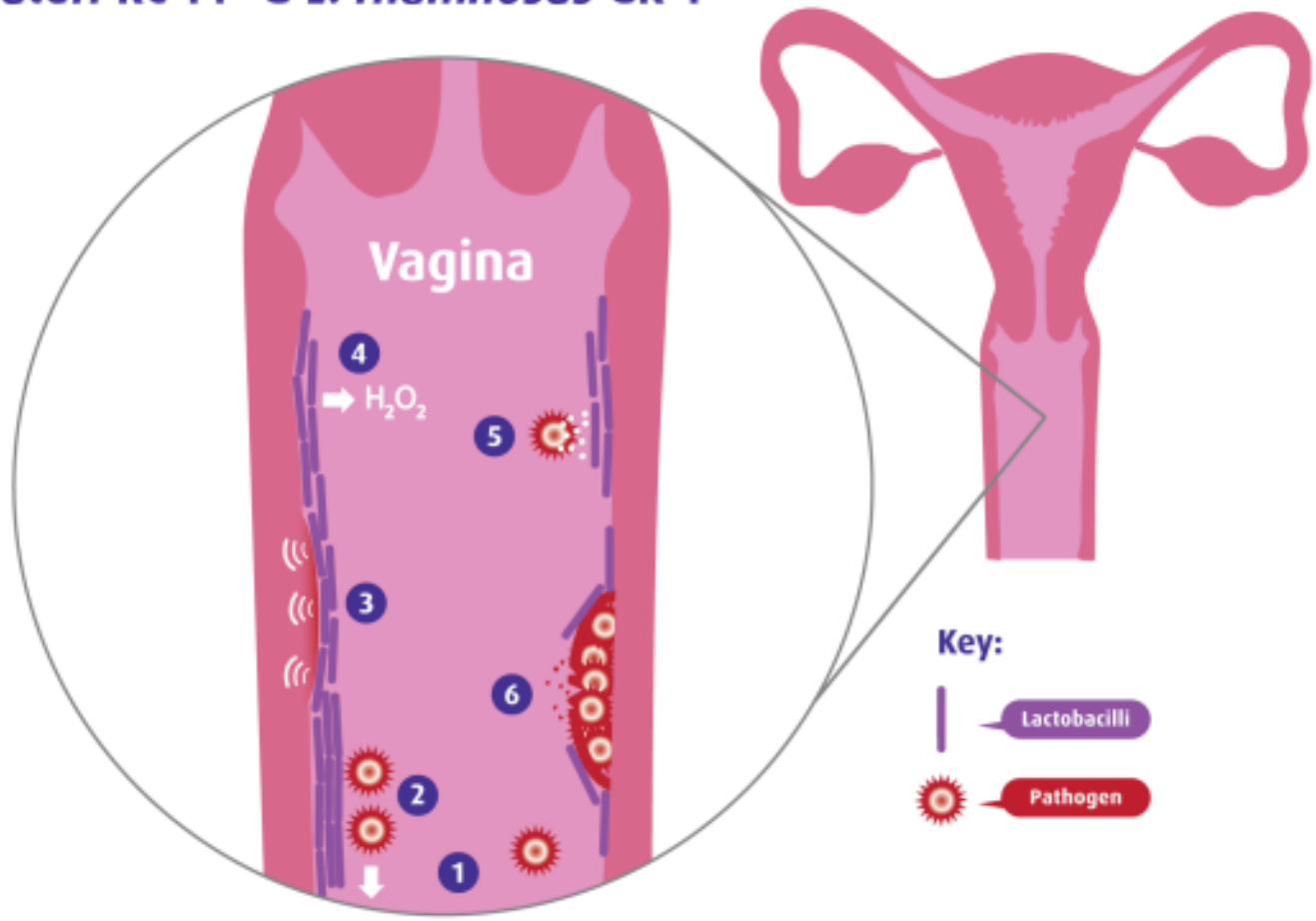


Figure 1
Influential factors on the maternal and infant microbiota. Maternal factors significantly contribute to the initial colonization and succession of the infant gut microbiota. Alterations in this process may have long-term health consequences related to host metabolism and immune education. HMOs, human milk oligosaccharides; NAFLD, nonalcoholic fatty liver disease.

Mechanisms of action of *L. reuteri* RC-14® & *L. rhamnosus* GR-1®

1. Restores a healthy pH < 4.5
2. Competitive inhibition
3. Modulates cytokines to decrease inflammation
4. Produces H_2O_2 (kills pathogens and lowers pH)
5. Bacteriocin production (kills pathogens)
6. Produces biosurfactants, which breakdown pathogen biofilms

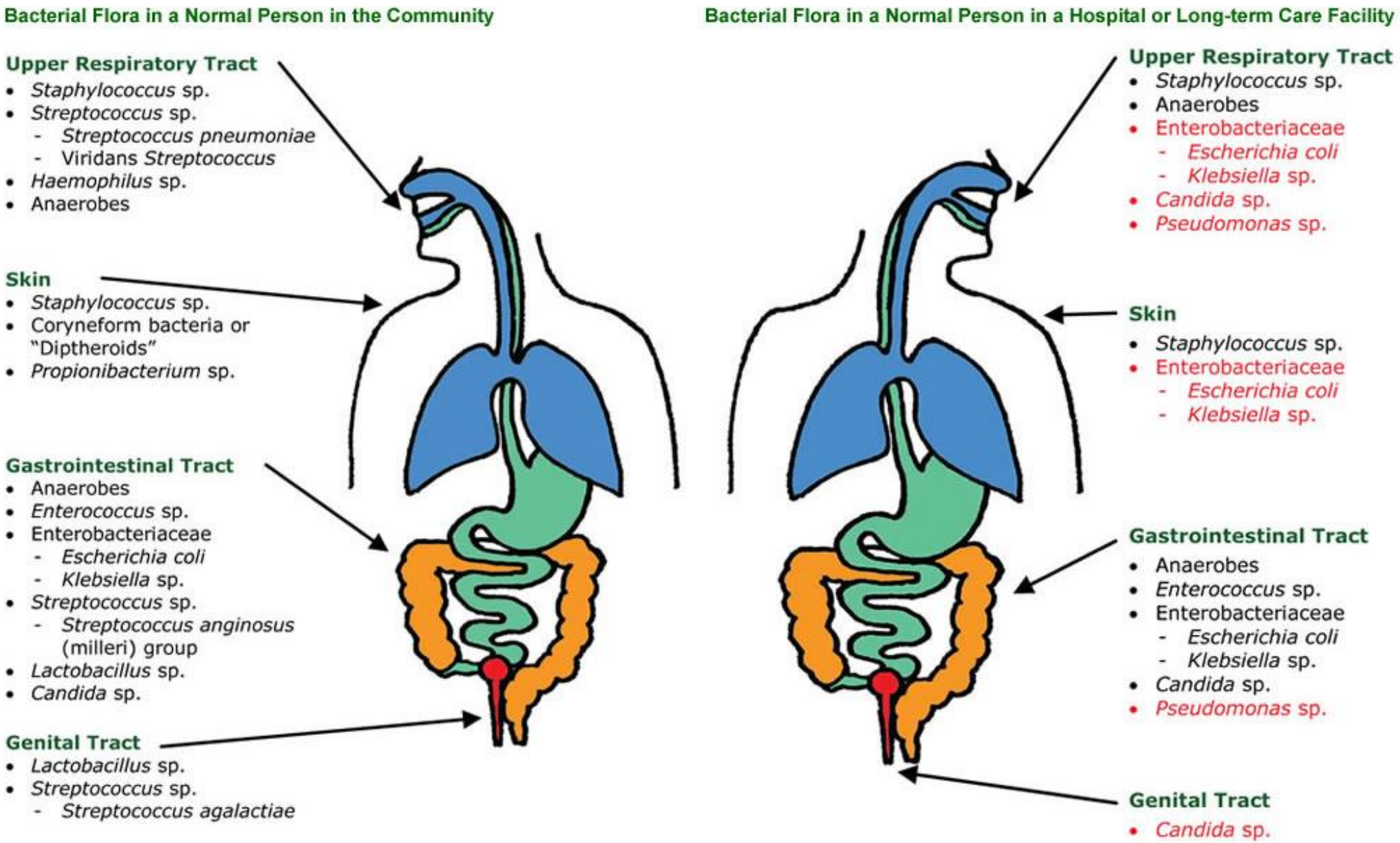


Taken from a website promoting probiotic therapy, proceed with caution!

- The disruption of the normal balance of the microbiota is known as:

- a) Dysbiosis
- b) Homeostasis
- c) Symbiosis
- d) Eubiosis

Microbiota variation in health and disease



Learning outcomes

For today's lecture on human microbiota, here are four potential learning outcomes:

1. **Describe the Composition and Diversity of Human Microbiota**: Understand the various microorganisms that comprise the human microbiota, including bacteria, fungi, viruses, and archaea, and their distribution across different body sites.
2. **Explain the Role of Microbiota in Health**: Analyze the essential functions of the microbiota in maintaining physiological processes, such as digestion, immune modulation, and protection against pathogens.
3. **Identify the Impact of Dysbiosis on Disease**: Discuss how imbalances in the microbiota (dysbiosis) are associated with various health conditions, including gastrointestinal disorders, metabolic diseases, and immune dysfunction.
4. **Explore Factors Influencing Microbiota Composition**: Recognize factors that affect microbiota diversity and stability, such as diet, antibiotic use, environment, and lifestyle, and their implications for maintaining a healthy microbiome.

Further reading and material:

- The human microbiome project
www.hmpdacc.org

- Jawetz, Melnick & Adelberg's Medical Microbiology, 26th edition-
  Section 3: Bacteriology
    Chapter 10: Normal human microbiota