Microbiome Analysis in Lithuania: Overview of the Global and Local Ecosystem, Strengths, Weaknesses, and Recommendations

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Microbiome Terminology and Importance

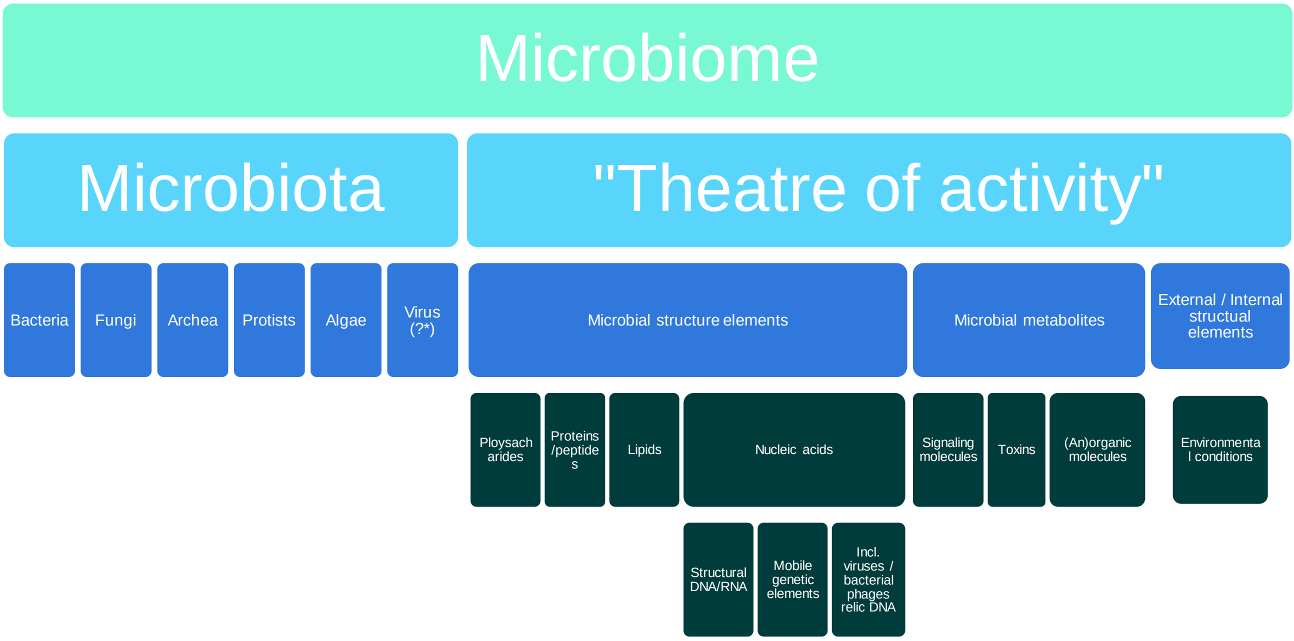
Microbiome Terminology

The microbiome refers to the collection of trillions of bacteria, viruses, yeast, fungi, and archaea, including their genetic material, and their interactions inside and on a host organism or environment.[1]

While the term 'microbiome' broadly encompasses the diverse microorganisms within a host, the distinction between the terms 'microbiota' and 'microbiome' is often misunderstood or used interchangeably. Microbiota describes the living microorganisms found in a defined environment, such as oral and gut microbiota.[2] The microbiome refers to the collective genomes of all microorganisms within a given environment. This includes not only the microbial community, known as the microbiota, but also their "theater of activity," which encompasses structural components, metabolites, signaling molecules, and surrounding environmental conditions. In this sense, the microbiome represents a broader concept than microbiota, capturing both the organisms and their dynamic interactions within their habitat.[3] Understanding these distinctions is essential, as the microbiome's influence reaches beyond individual hosts to impact entire ecosystems and the interconnected health of humans, animals, and the environment.

Figure 1

Microbiome Terminology Components



Note: prepared by the authors, based on Xia & Sun, 2023[4]

[1] https://op.europa.eu/en/publication-detail/-/publication/69446d55-1f41-11ec-bd8e-01aa75ed71a1/language-en

[2] https://doi.org/10.1038/s41392-022-00974-4

[3] https://doi.org/10.1016/b978-0-323-98338-9.00001-3

[4] https://doi.org/10.1016/b978-0-323-98338-9.00001-3

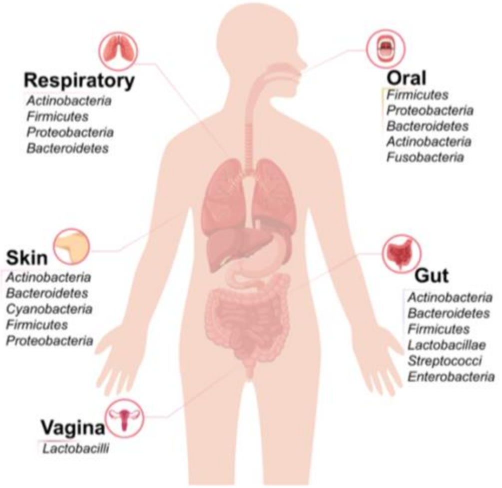
The Role of the Microbiome in Human Health

The composition and distribution of the human microbiome vary from person to person. It is influenced by genetic factors as well as environmental conditions, including diet and medication use. Bacteria make up approximately 99.9% of the human microbiome, while fungi, viruses, and phages collectively account for less than 0.1%.

Within the human body, the gut microbiome composes about 95% of the total human microbiome and is considered to be the most important one for maintaining health.[5] The second largest microbial community is the oral cavity, which includes smaller habitats, including the tongue, gums, and palate habitats. The rest of the human microbiome is made up of the skin, nose, respiratory, and vagina microbiomes, all of which have unique compositions of microbiota.[6]

Figure 2

Microbiota Composition in the Human Body



Note: source from Hou et al., 2022.[7]

The human microbiome plays a crucial role in various processes:

Microbiome and its Role in Digestion and Metabolism

Microbiota in the gut play a vital role in digestion and metabolism by breaking down complex carbohydrates and dietary fibers that the body cannot process by itself. This breakdown produces short-chain fatty acids (SCFAs), which are essential nutrients that help nourish the cells lining your gut, promoting a healthy digestive environment.

In addition to their role in digestion, gut bacteria provide enzymes necessary for synthesizing important vitamins such as B1, B9, B12, and K. Though small in quantity, these micronutrients are critical, as deficiencies in them can lead to significant health issues, including vitamin B12 deficiency, folate deficiency, and vitamin K deficiency.

Moreover, gut bacteria assist in metabolizing bile in the intestines. When the liver releases bile to aid in fat digestion, bacteria break down the bile acids, allowing them to be reabsorbed and recycled. This recycling process

[5] https://op.europa.eu/en/publication-detail/-/publication/69446d55-1f41-11ec-bd8e-01aa75ed71a1/language-en

[6] https://doi.org/10.1038/s41392-022-00974-4

[7] https://www.nature.com/articles/s41392-022-00974-4

is vital because, without it, the body wouldn't have enough bile to digest fats properly, and cholesterol could build up in the bloodstream, leading to potential health problems.[8]

Considering the vital role gut bacteria play in these processes, it's evident that preserving a balanced gut microbiome is essential. Dysbiosis refers to a disruption in the gut microbiome, defined as the imbalance of microorganisms in the body. This is characterized by the loss of beneficial microorganisms, the overgrowth of potentially harmful bacteria, and a decrease in overall microbial diversity.[9] Dysbiosis can trigger low-grade systemic inflammation, which elevates the risk of obesity and metabolic diseases.[10] Additionally, it has been associated with various chronic diseases, including gastrointestinal, inflammatory, metabolic, neurological, cardiovascular, and respiratory illnesses.[11]

The gut microbiota also impact functions in the brain and skin through the gut-brain axis and gut-skin axis, which will be explained further in detail.

Microbiome and its Role in the Immune System

Microbiota regulate the immune system and maintain balance (homeostasis) by producing cytokines and T cells, which are essential for potecting the body against pathogens. The microbiome interacts closely with the immune system and is strongly influenced by environmental factors during birth and infancy. It also plays a role in the development of certain immune system components, such as myeloid cell derivatives, suggesting that microbiota influence immune cell differentiation and the effectiveness of immune responses.[12]

Environmental factors, particularly diet and antibiotics, significantly impact the microbiome. Diet alters the microbiota and, in turn, alters T cell responses to microbes. Antibiotics decrease the level and diversity of the microbiota, reducing the efficacy of the immune response.[13]

Microbiome and its Role in Mental Health

The microbiome plays a crucial role in mental health through the gut-brain axis, which is the bi-directional communication between the brain and gut microbiome. In addition to regulating cortisol and amino acid pathways, the gut microbiota produce neurotransmitters and short-chain fatty acids (SCFAs) which promote mental health well-being. In turn, the brain affects the gut microbiota by modulating gut functions and secreting signaling molecules, which affect the health and functions of bacteria in the gut.[14]

Therefore, an imbalance in the gut microbiome directly affects the brain. The abundance or scarcity of several microbiota is linked to mental health illnesses including depression, anxiety, and bipolar disorder.[15] Neurodegenerative diseases, such as Alzheimer's and Parkinson's, are also correlated with dysbiosis. There is growing support and research to use microbiota-based treatments for these conditions.

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[8] https://my.clevelandclinic.org/health/body/25201-gut-microbiome

[9] https://doi.org/10.1093/advances/nmy078

[10] https://doi.org/10.1016/j.biopha.2022.112678

[11] https://doi.org/10.1038/s41430-021-00991-6

[12] https://doi.org/10.1615/critrevimmunol.2019033233

[13] https://doi.org/10.3390/nu11122862

[14] https://pmc.ncbi.nlm.nih.gov/articles/PMC4367209/

[15] https://doi.org/10.3390/nu15143258

Recent research has demonstrated that prebiotics and probiotics, which contain beneficial bacteria, can alter the microbiome to treat mental health disorders. These are known as psychobiotics, and evidence suggests that they potentially have positive effects on mood, cognition, and anxiety. For example, probiotics like *Lactobacillus* secrete gamma-aminobutyric acid (GABA), which leads to reduced depression-like symptoms. Therefore, incorporating probiotic-rich foods into the diet may support mental health by boosting beneficial bacteria and reducing harmful ones.[16]

Microbiome and its Role in Cancer

The microbiome is increasingly associated with its role in cancer. Certain strains of bacteria are associated with colorectal cancer, gastric cancer, lung cancer, breast cancer and serve as biomarkers for early diagnosis and prevention. An earlier diagnosis is crucial to increasing survival rate and being able to develop personalized interventions.[17]

It is essential to also consider the effects cancer treatments can have on the microbiome itself. Chemotherapy and immunotherapy in cancer treatment heavily alter the microbiome, increasing harmful bacteria and reducing beneficial bacteria, leading to cognitive impairment and neuroinflammation. This dysbosis can also lead to tumor progression.[18]

Researchers have found potential in altering microbiota to better respond to cancer treatments. One method is by using antibiotics targeted towards the carcinogenic microbiota. Although antibiotics are generally harmful towards the microbiome and are related to poor clinical outcomes for cancer patients, antibiotics targeted towards specific microbiota may assist in improving clinical outcomes and cancer prevention by killing harmful bacteria. Another method is genetically modifying bacteria in the microbiome to enhance their anti-cancer activity.[19] This strategy restores the balance of beneficial bacteria and can lead to improved clinical outcomes for cancer patients.

Microbiome and its Role in Skin Health

The skin, our largest organ, acts as a barrier against external threats. The skin microbiota assist in this protection by secreting molecules to kill pathogens.[20] However, disruptions in gut microbiome diversity can weaken this defense, affecting immune tolerance and skin health. Gut dysbiosis triggers immune responses and is linked to conditions such as acne, allergies, atopic dermatitis, psoriasis, and rosacea.

This connection between the gut and skin is called the gut-skin axis, which explains how gut microbes influence skin health through immune and metabolic processes, such as regulating the function of immune cells.

Diet plays a major role in this relationship: high-fat diets decrease microbial diversity and increase the production of lipopolysaccharides, leading to inflammation and a higher risk of allergic diseases and skin conditions. In contrast, high-fiber diets promote beneficial bacteria and reduce inflammation. Additionally, consuming prebiotics and probiotics improves anti-inflammatory responses by supporting positive microbial populations in the gut.[21]

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[16] https://doi.org/10.1007/s12031-022-02053-3

[17] https://pmc.ncbi.nlm.nih.gov/articles/PMC10376920/

[18] https://doi.org/10.3390/microorganisms12010024

[19] https://doi.org/10.1038/s41392-023-01406-7

[20] https://pmc.ncbi.nlm.nih.gov/articles/PMC7444652/#:~:text=A%20recently%20recognized%20essential%20function,antimicrobial%20peptides%20and%20other%20molecules.

[21] https://doi.org/10.1080/19490976.2022.2096995

Microbiome and its Role in Maternal and Infant Health

The microbiome plays a crucial role in both maternal and infant health. During pregnancy, dysbiosis of the gut microbiome can lead to adverse outcomes, including gestational diabetes, preeclampsia, and restricted fetal growth.[22]

Several factors influence the health of the infant's microbiome. For example, the mode of delivery significantly influences the microbiome composition. Babies born vaginally are exposed to their mother's vaginal and gut microbiota, which helps develop a microbiome that supports immune development. In contrast, infants born via cesarean section often develop a microbiome more similar to their mother's skin microbiome, which may negatively impact their immune system and increase the risk of allergies, asthma, and autoimmune disorders.[23]

Breastfeeding also plays a key role in infant health by providing beneficial bacteria, such as Bifidobacterium, which nourish the gut microbiota. This support is vital for promoting a healthy microbiome and fostering stronger immune development, ultimately laying the groundwork for the infant's long-term health.[24]

As the infant grows, their microbiome becomes more diverse with increased exposure to the environment. By the age of 3, the child's microbiome follows similar patterns to an adult's microbiome. In adolescence, the microbiome continues to increase in stability and diversity. During these stages of development, environmental factors such as diet, antibiotic use, and living space heavily influence the composition and health of the microbiome.[25]

In older age, the composition of the microbiome also undergoes major shifts. Unhealthy ageing is associated with decreased variability in the microbiome and a reduction in beneficial species, which are crucial in maintaining homeostasis.[26]

Microbiome and its Role in COVID-19

Coronovirus disease (COVID-19) susceptibility, severity, and outcomes have been linked to an altered and less diverse gut microbiome. Increased levels of *Enterococcus* and *Enterobacteriaceae* bacteria are associated with increased severity of infection, while the abundance of probiotic bacteria, such as *Bifidobacterium*, decreases as COVID-19 severity increases.[27]

Studies have also shown that patients treated with antibiotics experienced more significant disruptions to their microbiomes, as well as more severe COVID-19 outcomes. In patients with long-term illness, microbiome dysbiosis persisted for a longer period. Additionally, there is evidence that changes in the gut microbiome can lead to changes in the bloodstream, potentially increasing the risk of bloodstream infections.[28] The primary challenge is determining if the dysbiosis was due to COVID-19, or is the effect.

Several microbiome-based treatments, including dietary changes, fecal microbiota transplantation, probiotics, prebiotics, and microbiota-derived metabolites, have shown beneficial outcomes in clinical trials against COVID-19. Oral probiotics and prebiotics, in particular, have been found to boost antiviral activity, increase gut microbial

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[22] https://doi.org/10.3389/fcimb.2022.824925

[23] https://doi.org/10.3390/microorganisms8101587

[24] https://hms.harvard.edu/news/diet-gut-microbes-immunity

[25] https://pmc.ncbi.nlm.nih.gov/articles/PMC8714606/#:~:text=During%20childhood%20years%20the%20diversity,species%20(113%2C%20114)

[26] https://doi.org/10.1038/s41575-022-00605-x

[27] https://doi.org/10.3389/fimmu.2023.1180336

[28] https://doi.org/10.1038/s41467-022-33395-6

diversity, and improve recovery in COVID-19 patients. Microbiome-based approaches not only hold promise for preventing or treating COVID-19 but could also enhance the efficacy of vaccines.[29]

COVID-19 has also affected infants born during the pandemic. An analysis revealed differences in microbiome diversity between infants born before and during the pandemic, and other studies demonstrated that the risk of childhood conditions such as obesity, myopia, and mental health disorders increased during this period.[30]

Environmental Microbiome

The environmental microbiome is fundamental to the stability of ecosystems, driving processes such as nutrient cycling, climate regulation, and soil fertility. [31]

Nutrient Cycling in Soil

One of the primary roles of microbial diversity in ecosystems is in nutrient cycling. Nutrient cycling in soil involves the transformation and movement of essential elements such as carbon, nitrogen, phosphorus, and sulfur. Soil microbes are pivotal in these cycles, mediating processes that convert nutrients into forms accessible to plants and other organisms.

Figure 3

Nutrient Cycling in Soil

Carbon Cycle	Nitrogen Cycle	Phosphorus Cycle	Sulfur Cycle
• Microbiota decompose organic matter into simpler compounds and release carbon dioxide through respiration • Bacteria recycle carbon and produce humus, which improves soil structure and fertility	• Soil microbes convert atmospheric nitrogen into ammonia through nitrogen fixation • Other bacteria then transform ammonia to nitrites and nitrates, which plants ingest as nutrients • Denitrifying bacteria turn nitrates back into nitrogen gas, preventing excess nitrogen buildup in the soil	• Bacteria and fungi in the soil help release phosphorus from organic and inorganic sources, making it accessible to plants • *Mycorrhizal* fungi form symbiotic relationships with plant roots, improving phosphorus and nutrient absorption	• Sulfur-oxidizing bacteria in the soil convert sulfides into sulfate, which plants then absorb to make amino acids and proteins • Sulfate-reducing bacteria then change sulfate back into sulfide

Note: source from Ruikar et al. (2024).[32]

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[29] https://doi.org/10.1038/s41575-022-00698-4

[30] https://doi.org/10.1038/s41575-022-00698-4

[31] https://doi.org/10.48047/AFJBS.6.Si1.2024.198-216

[32] https://www.afjbs.com/uploads/paper/b81b1ed007342ac572735500a7c1c6b3.pdf

Climate Regulation

Microbiota play a crucial role in climate regulation through their involvement in biogeochemical cycles and greenhouse gas dynamics. Photosynthetic microorganisms help mitigate climate change by converting carbon dioxide into organic carbon, and other microorganisms contribute to global warming by producing methane or nitrous oxide, potent greenhouse gases.

Soil Health and Erosion Prevention

Soil microbes facilitate nutrient cycling and improve soil health by decomposing organic matter, leading to humus formation. Humus enhances soil texture, water retention, and aeration, supporting root growth and nutrient availability, benefiting plant health and productivity. Additionally, microbial exudates, such as polysaccharides, bind soil particles, forming stable aggregates that reduce erosion and improve soil stability.

However, human activities like intensive agriculture, deforestation, pollution, and climate change can harm them, leading to soil degradation and reduced fertility. Overuse of fertilizers and pesticides, as well as land conversion, disrupts microbial communities, reducing their ability to decompose organic matter and cycle nutrients.

To counteract these negative impacts, sustainable practices like crop rotation, organic farming, reduced tillage, and cover crops can help restore microbial diversity, promoting nutrient cycling, improve soil structure, overall health, and enhance fertility.[33]

Human-Environmental Microbiome Interactions

The One Health Concept

Human and environmental health is closely interconnected and dependent on one another. One Health is a concept that describes this relationship between the human, animal, and environmental microbiomes. Changes in the environment, such as warming temperatures, alter the soil microbiome's physical and chemical composition, leading to less nutrient-rich food, and therefore a less diverse microbiome in both humans and animals. This negatively affects human and animal health by increasing disease susceptibility.[34] In turn, human activities such as urbanization and pollution hurt the environmental microbiome by lowering soil microbial diversity. It also negatively impacts animal health, with habitat loss. This leads to an increase in soil-borne pathogens, which then negatively affect the health of animals and humans who are exposed to that soil microbiome.[35] Emphasizing the importance of the connection between human and environmental microbiomes and increasing collaboration between these sectors is crucial to improve human, animal, and environmental health.

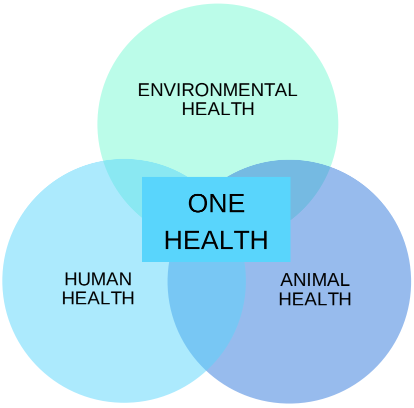
[33] https://www.afjbs.com/uploads/paper/b81b1ed007342ac572735500a7c1c6b3.pdf

[34] https://www.sciencedirect.com/science/article/pii/S2949704323000318?via%3Dihub

[35] https://doi.org/10.1038/s41579-022-00779-w

Figure 4

One Health Principle



Note: prepared by authors based on the Destoumieux-Garzón et al., 2018.[36]

The One Health Joint Plan of Action seeks to unite countries on an actionable strategy to achieve the 2030 Sustainable Development Goals (SDGs) through One Health approaches. The goals related to human health are SDG 1 (No Poverty) and SDG 3 (Good Health and Well-Being). The environmental related goals are SDG 6 (Clean Water and Sanitation), SDG 13 (Climate Action), SDG 14 (Life Below Water), and SDG 15 (Life on Land). The health of all living systems is covered by SDG 2 (Zero Hunger) and SDG 11 (Sustainable Cities and Communities), and SDG 17 (Partnerships for the Goals) is crucial for the implementation of the One Health approach. Understanding the interconnectedness of all living systems under the One Health perspective is critical to achieving the SDGs. By fostering interdisciplinary collaboration and sustainable practices, this approach lays the foundation for solutions to global health and environmental challenges.[37]

Figure 5

Sustainable Development Goals through the One Health Approach

Note: source from One Health and the United Nations Sustainable Development Cooperation Framework, 2023. [38]

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[36] https://www.researchgate.net/publication/322642012_The_One_Health_Concept_10_Years_Old_and_a_Long_Road_Ahead

[37] https://doi.org/10.4060/cc5067en

[38] https://doi.org/10.4060/cc5067en