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**Review** Article

# Microbiota as a linking axis of the macroecosystem involving soil-plant-human. Potential interactions and perspectives for study

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During analyzing morbidity data, it is obvious that the ratio of infections has decreased significantly since the beginning of the 20<sup>th</sup> century, but the proportion of metabolic and inflammatory diseases has increased. This may be related to the degradation of soils. At the same time, mobilization of nutrient elements primarily depends on the activity of soil microbiota, which is subjected to negative anthropogenic impact. Although plant nutritional value has a direct impact on human health; however, modern agricultural practices that aimed at deep cultivation are causing disturbances in the soil microbiota composition. Subsequently, this resulted in maladaptation of the human immune system, as contacts with xenobiotics occur instead of evolutionarily calibrated interactions; potentially endangering the gut microbiota. This review aims to represent recent data on the relationships among human intestinal, soil, and plant microbiota. Nowadays, it is evident that there is a broad range of influences on human health not only from intestinal microbiota but also from its connection with the environmental microbiota (i.e., soil microorganisms in particular). Today, with respect to the background of active use of modern technologies, including genetical ones, we have the opportunity to examine such volumes of data that will allow us to fully analyze microbiological diversity of the different ecological niches in terms of their common features, differences, and mutual influences. Such studies will make it possible to identify potential factors determining the composition of microbiota in different loci, assess their potential impact on human health, and adjust methods to diagnose and restore the optimal composition of human, plant, and soil microbiota.

Keywords: Human microbiota, Plant microbiota, Soil microbiota, Ecological microbiology

## 1. Introduction

Exploration of the microorganisms' significance has changed the human attitude to all spheres of activity (Gupta *et al.*, 2016). First of all, it concerns human intestinal microbiota; however, less intensive researches on microbiota of soil, water, plants, and other kinds of loci are going on now. The previous studies dedicated to microorganisms, colonizing environment, and microorganisms of human body were carried out for a long time individually, but recently their interrelation has become more obvious (Hirt, 2020).

Initially, the relationship between human and soil microbiota was considered only in terms of pathogenicity. However, as certain amount of data has accumulated, it becomes evident that microbiota directly determines the ecological balance in soil; including arable lands, and, consequently, establishes the nutritional value of food and its benefits to human health. On the other hand, the anthropogenic activity can negatively affect the condition of soil microbiota, and thereby the quality of food and human health (Samaddar *et al.*, 2021).

Despite the obvious link between human and environmental microbiota, this interaction has only begun to be investigated in the last decade; particularly within the framework of "One health concept" (Destoumieux-Garzón *et al.*, 2018). This approach allows us to consider the microbiota of all loci as a single ecological system or a single genome.

The "One health concept" emphasizes on the relationships among humans, plants, animals, and the environment. Until recently; however, this paradigm has focused only on pathogens, viral vectors, and antibiotic resistance. In the last decade, meanwhile, it has become evident that microbial communities also play a positive role within this interaction, as an integral component of the nutrient chain on one hand and as participants in vital metabolic processes on the other hand <u>(van Bruggen *et al.*</u>, 2019).

The evidence is now growing that human microbiota has primarily been shaped under the influence of environment (Panthee et al., 2022). And today, along with the development of new sequencing technologies, it becomes possible to study those microorganisms that are difficult or impossible to cultivate. Identification of these microorganisms gives a possibility for more detailed studies on the relationship between humans and environment, which is especially relevant due to polarization of urban and rural residents, in addition to their fundamental different interaction with nature (Panthee et al., 2022). The objectives of this study are to emphasize the connections among microbial communities of human body, plants, and soils, and find out negative factors, which can disturb this interaction among such communities in modern conditions.

## 2. The concept of "soil-plant-gut microbiota"

Microbial colonization of the human intestine begins immediately after birth and is caused by both endogenous (genes) and exogenous factors (*i.e.*, nutrition, infections, xenobiotics, consumption of food, and soil microbiota) (Gilbert *et al.*, 2018). Considering the importance of such factors, several studies revealed that diet has a greater influence on composition of the intestinal flora compared to genetics (Matute and Iyavoo, 2023). Moreover, other studies showed that gut microbiota can influence the host genetic mechanisms by regulating the expression of some genes responsible for energy metabolism (Rowland *et al.*, 2018).

These findings were confirmed by a previous study conducted by Rothschild et al., (2018) where the gut microbiota of over 1000 healthy individuals was examined (Rothschild et al., 2018). According to the obtained results, the intestinal microbiota of relatives who lived away from each other differed significantly compared to people with no blood relation but living close to each other. Such facts have proven that the endogenous microbiota is assembled primarily by exogenous factors. In particular, Kurilshikov et al., (2017) study demonstrated that there are certain «basic» groups of microorganisms typical for certain types of soils, which directly correlate with the groups of intestinal microorganisms of people living in this area. The proportion of these microorganisms represents about 8 %, while the rest are assembled under the influence of individual lifestyle and other exogenous factors.

However, up to date, there are still a small number of studies on the differences between microbiota of urban and rural residents. In 2022, one of the first cohort studies involving 56 participants was published by Brown et al., (2022), where fecal, soil, food, and questionnaire samples were analyzed in different seasons. It was found that at the peak of gardening season, the comparison groups differed significantly in both of the number and composition of the gut microbiota. In particular, there was a predominance of Bacteroides ovatus (p = 0.02) and Eubacterium xylanophilum (p = 0.02) in rural residents. of Furthermore, representatives the Alphaproteobacteria class and undetectable taxa predominated in 64 % of residents inhabiting rural areas. The statistical significance of the obtained results showed the necessity for further research and assessment of the identified differences in significance in terms of its impact on human health (Bu et al., 2024). It is well-known that gut microbiota fulfills a range of essential functions, from metabolic to immunological ones. Today, it is widely believed that disturbances in normal composition of the intestinal

microbiota are associated with the emergence of several diseases such as diabetes mellitus, autoimmune disorders, inflammatory bowel diseases, psoriatic arthritis, eczema, celiac disease, etc. (Zhang *et al.*, 2021). Therefore, during the last decades, the possibilities of influencing the gut microbiota through pre-, pro-, and metabiotics have been actively investigated; however, nowadays another trend is gaining popularity that is the influence on microbiota *via* the environment (Bu *et al.*, 2024).

In particular, a study was conducted by <u>Kirjavainen</u> et al., (2019), where the microbiota of two groups of children was examined (*i.e.*, one group was actively interacting with soil and plants whereas children from the second group were living in urban area and thereby did not have much contact with soil). The obtained results expressed that the metabolic pathways regulating an adequate immune response were more developed in the first group of children. In addition, the study reliably showed a lower risk of bronchial asthma emergence upon exposure to natural environment.

Considering the aforementioned points, a comprehensive understanding of human health requires an analysis of transmission mechanisms of both pathogenic and beneficial microorganisms under specific macroecological conditions, including nutrition and lifestyle in contact with the environment (Mendes and Raaijmakers, 2015).

## 3. Similarities among soil, plant and gut microbiota

The human gut microbiome is a complex system that consists of billions of bacteria, fungi, viruses, and protozoa that have a huge impact on the human body. The same is true for the rhizosphere of plants, as the microbiota of the root zone performs vital functions in terms of defense against pathogens, nutrient mobility, and tolerance to changes in environmental conditions (Pantigoso *et al.*, 2022).

The significance of the microbiota for plant biology has been known for a long time. Five main

functions are generally emphasized; mainly 1) facilitation of nutrient acquisition, 2) maintenance of plant growth and defense against biotic and abiotic stresses, 3) protection against pathogens, 4) interaction with soil microbiota, and 5) interaction with representatives of other trophic levels (Berg *et al.*, 2014). Similar to the gut microbiota of animals, the plant microbiota also depends on species, genotype, and environmental factors, which varies in different organs and tissues (*i.e.* leaves, roots, and fruits), and also changes gradually during life cycle of the plant (Wagner *et al.*, 2016).

However, despite the apparent interaction and functional similarities between the gut and soil microbiota; however, they have very little similarities in common in terms of composition. A study was conducted to compare the gut and soil microbiota, which revealed that human feces were dominated by Bacteriodetes and Firmicutes, while soil samples were dominated by Proteobacteria and Verrucomicrobia. Although limited data are now available for the different geographical areas, it is clear that there are quite strong differences between the two communities (Blum et al., 2019). This is primarily attributed to the fact that soil has a limited amount of available carbon and high number of soil microorganisms that actually have to struggle for survival. The opposite case is in the human gut, where carbon and other nutrients are abundant. This can be assigned to the fact that evolution of plants and animals has taken two different directions. For example, plants are autotrophic synthesize carbohydrates and by themselves, which are used for nutrition and building of the plant. In turn, they limit the amount of nutrients available for the microbiota (Blum et al., 2019). However, the situation is different in the plants rhizosphere, where endophytic the microbial community exists. In this zone, abundances of root exudates are observed that create special conditions for the microorganisms. In particular, high prevalence of Bacteriodetes typical for intestinal microbiota has been detected in the rhizosphere of red clover along with nodular bacteria (Blum, 2017).

In addition to certain similarities in microbiological composition, there are functional associations between rhizosphere and intestinal microbiota. Firstly, both the gut and the rhizosphere are open systems with a large and a diverse surface area population of microorganisms (Blum et al., 2019). Secondly, in both of the gut and the rhizosphere there is a gradient of oxygen, water, and pH, forming niches for microorganisms that differ in their composition. In addition, definite physiological processes in above mentioned loci have a tendency to change their intensity along with circadian rhythms. For example, nitrogen fixation by bacteria is more pronounced during the daytime, while concentration of the intestinal melatonin, on the contrary, increases at night (Rowson et al., 2024). Such functional similarities between the two types of microbial communities may provide a basis for development of pathogen control strategies. In particular, a clear inverse correlation between pathogen survival rates and host microbiota biodiversity has been demonstrated in both plants and animals (Wicaksono et al., 2023). The reason for this an active competition for resources, and is consequently, a more advantageous position for the host microbiota is attributable to their adaptation.

On the other hand, the existing differences in composition of the gut and rhizosphere microbiota will not allow creating quick simple solutions for these problems. In addition, it is necessary to study not only the differences between such communities, but also within them (*i.e.* between individual species), as a result of several exogenous (in particular anthropogenic) factors, including urbanization as a factor affecting humans, and agriculture affecting plants.

#### 4. Microbiota, urbanization and immunity

Modern urbanized society has lost contact with the environmental microbiota, which has a negative impact on human health; particularly in terms of allergic and autoimmune diseases. Our ancestors lived in close contact with environmental microorganisms and today retrospective studies proved that children living in rural areas are less likely to suffer from autoimmune disorders and allergies (Khan and Wang, 2020).

Nowadays, a certain number of original studies have been conducted to prove these trends. In particular, a research using 16s RNA genetic sequencing has examined the intestinal microbiota of two groups of mice, one of which lived in sterile conditions while the other in close contact with soil (Zhou et al., 2016). It was found that the soil group has had a higher ratio of Bacteroidetes to Firmicutes, and showed higher expression of immunoregulatory markers, including IL-10, FOX\_P3 protein and cvtotoxic T-lymphocyte associated protein 4. Furthermore, using an experimental model of bronchial asthma, it has been demonstrated that the second group has a predominant expression of genes of anti-inflammatory signaling pathways. This study along with similar ones, also deals in favor of the hypothesis that soil microbiota is able to regulate the immune response (Edwards et al., 2021).

In another study conducted by Zhou et al., (2022) on mice, four groups were examined: the first group was kept in sterile conditions; the second group lived in contact with soil containing small amounts of microorganisms; the third group received microorganisms with food; and the fourth group lived in contact with normal soil. Metagenomic analysis revealed that the second group, simply inhaling air containing soil microorganisms, had increased gut microbiota biodiversity and decreased IgE levels. In the third group, the number of genes related to the metabolism of short-chain fatty acids and amino acids synthesis was increased. In the fourth group, all the above changes were observed; however they were even more pronounced. Therefore, the results of this study showed that soil may serve as a potential source of probiotics that can be used in treatment of allergic and autoimmune diseases. Considering that such pathologies are becoming increasingly common in modern society, there is an active search for alternative methods to be used for diseases treatment and prevention (Bhattacharjee et al., 2023). The role of intestinal microbiota in establishment of immune tolerance has been studied for a long time, and today researchers have started to evaluate the role of soil in the formation of immune disorders affecting the human population.

Understanding the influence of soil microbiota on immunity is of particular relevance today, because urbanization has forced citizens to lose contact with the microbiota of natural ecosystems, which can have a negative impact on human health (Flandroy *et al.*, <u>2018</u>). As mentioned before, this applies primarily to allergic and autoimmune diseases within the concept of "One Health" and "Hygiene hypothesis", accordingly children in rural areas are less susceptible to immunity impairments.

It should be noted that immune tolerance is promoted by contact not only with neutral bacteria but also with potentially pathogenic ones. In particular, the influence of contact with soil mycobacteria has been investigated so far and a conclusion has been drawn about their positive influence on an adequate immune function (Divangahi *et al.*, 2018). This is especially crucial in terms of assessing the role of vaccination on immune tolerance, rather than just specific immune response.

Appreciable amounts of structural components of the normal microbiota release bioactive molecules, which interact with the host physiological pathways (Postler and Ghosh, 2017) and regulate the organs development, including the nervous system and metabolism. These active molecules include shortchain fatty acids, tyrosine, and/ or tryptophan metabolites, which play an important role in regulating the immune and neuroendocrine systems (Erdman and Poutahidis, 2017). These substances have been shown to promote T-lymphocyte activation, reduce the activity of pro-inflammatory cytokines, and promote the secretion of anti-inflammatory hormones (Carabotti *et al.*, 2015).

Furthermore, it has been shown that a number of microorganisms that have been subjected to heat

retain the ability to exert positive effects on human physiology (Reber *et al.*, 2016), which clarify the increasing popularity that metabiotics are gaining in clinical medicine (Jang *et al.*, 2024). This described phenomenon is not limited to the gastrointestinal tract, as similar immunomodulatory effects have been observed for inhaled air (Schuijs *et al.*, 2015). Lipopolysaccharides of Gram-negative bacteria can reduce allergic responses in human body (Tanaka *et al.*, 2022).

Therefore, there is increasing evidence that interaction with potential allergens and pathogens in the environment has a positive impact on the development of human immunity, whereas the "sterilized" urban life leads to disruption of the normal neuroendocrine function. An important role played in the prevalence of these trends has been observed not only by industrialization that affects humans directly, but also by intensive agricultural practices, which have a negative impact on the soil, plant microbiota, and as a consequence, on humans (Meena *et al.*, 2020).

#### 5. Agriculture and soil

As has been mentioned before, human gut microbiota is primarily determined by lifestyle and diet (Meena et al., 2020). Nutrient value of food products is consequently established by its production technology, *i.e.* agricultural practices, which have changed drastically over the last century (Donal et al., 2001). Today, as a rule, intensive technologies are used, which include deep ploughing, sowing of commercially profitable monocultures, and active use of herbicides and mineral fertilizers. This fact is the reason why most of the plants are losing their natural defensive properties. A vivid example is the changes that occurred to members of the Brassicacae family such as cabbage and cauliflower (Liu et al., 2021). As a result of intensive agricultural practices, the amount of glucosinolates has been significantly reduced in such plants. These substances not only perform a protective function, but also stimulate the human immune system and reduce the risk of cancer.

The cause of such changes may be attributed to the degradation of soil, which is a substrate from which plants obtain their necessary nutrients (Donal *et al.*, 2001). Nutrient acquisition is primarily driven by interactions with microbiota of the rhizosphere, leaves (phyllosphere), and other plant organs (endosphere). Soil and plant microbiota not only increases metabolic efficiency of its hosts, but also increases resistance to pathogens, insects, and fungi (Blum *et al.*, 2019).

A prime example of the negative human impact on soil ecology is the use of the herbicide glyphosate, which inhibits the enolpyruvylshikimate-5-phosphate synthase; an enzyme involved in biosynthesis of aromatic amino acids in plants. Although glyphosate has no direct toxic effects on humans; however, in 2015, it was recognized as a potential carcinogen by World Health Organization (WHO). On the other hand, glyphosate has negative effects on soil microorganisms, which along with plants use the prementioned enzyme to synthesize certain amino acids. In particular, a harmful effect on arbuscular mycorrhizal fungi and bacteria of the Rhizobium spp.; involved in nitrogen fixation, has been shown. Furthermore, in the intestine, glyphosate has been shown to inhibit the shikimate pathway in the beneficial taxa of *Bifidobacterium* spp. and Enterococcus spp. (Zhang et al., 2022).

In addition, the use of antibiotics in agriculture is becoming increasingly common. According to preliminary estimates, up to 20 times more antibiotics are used in agriculture than in medicine (Manyi-Loh <u>et al., 2018</u>). On the one hand, by analogy with the intestinal microbiota, antibiotics have a negative impact on bacteria that play a positive ecological role in the colonized locus. Moreover, trace amounts of antibiotics in plants can form resistant microbial strains both in the soil and humans, which require further research (Liao et al., 2021).

Today, as we witness soil degradation worldwide, the necessity to change the intensive agricultural practices and establish the use of alternative technologies is increasingly evident. One possible option might be the use of nature-like technologies in agriculture (Lorenzetti and Fiorini, 2024). This natural system of land use practices provides effective management of the biogenic elements cycle, produces natural processes to ensure plant protection, increases yields, and manages the soil ecological balance (Wittwer *et al.*, 2021).

Most food that we consume is produced at farms where herbicides, pesticides, and chemical fertilizers are used extensively in order to increase crop yields. However, such synthetic agents find their way into food as well, which worsen both the nutritional value and functioning of the gut microbiota. In this regard, biological treatments that contain beneficial soil microorganisms are being actively introduced today. Such strategies should reduce the amount of herbicides and pesticides reaching the human body (Lahlali *et al.*, 2022).

Food is the link between soil and human. In this regard, integrative studies on the microbiota of "soilplant-human" ecosystem are necessary. This knowledge will open new opportunities for diagnosis and treatment of diseases in humans and animals, and provides opportunities to find new methods of treatment through managing the impact of the microbiota.

#### Conclusion

For a long time, just like the gut microbiota, the soil microorganisms were considered only in terms of the possible "pathogenicity". However, at the moment, due to application of the latest metagenomic analysis and sequencing technologies, it is possible to study both ecosystems in greater depth. Firstly, direct analogies have been identified between the functions of the gut and soil microbiota for human and plant health in terms of their defensive potential against microbial pathogens. Other associations have been observed, including the ability of both types of microbiota to provide essential nutrients to their hosts through mobilization and synthesis of essential substances. Secondly, the composition of microbiota

has been shown to ensure soil and plant fertility, which directly affects the quality of agricultural products, and consequently human health, including their intestinal microbiota functioning. Thirdly, chemicals used in medicine and agriculture can mutually influence both soil and gut microbiota in terms of antibiotic resistance. To maintain the balance between the environmental and human microbiota, an integrated approach that takes into account the function of microorganisms in their natural habitat is needed. It is necessary to study the dynamics of microbial transition between the environment and and take measures humans to conserve microorganisms that play a positive role in promoting human health and ecosystem sustainability. In this regard, it is necessary to develop industries in all spheres based on nature-like technologies and change human lifestyle in general in the same direction. During analyzing morbidity data, it is obvious that the ratio of infections has decreased significantly since the beginning of the 20<sup>th</sup> century, but the proportion of metabolic and inflammatory diseases has increased. This may be related, according to some scientists, to the degradation of soils, which lose most of their nutrient elements. At the same time, mobilization of nutrient elements primarily depends on the activity of soil microbiota, which is subjected to negative anthropogenic impact. All this together leads to immunity disorders and increased morbidity despite significant progress in medicine as discussed above.

Progress in agricultural technology, which makes it possible to provide food for an ever-growing world population, cannot be dismissed out of hand. In this regard, it is necessary to foster a new concept of interaction with the environment, rather than return to the pre-industrial era. Thus, it will be possible to use the accumulated knowledge to find a new balance within the paradigm of an entire "soil-plant-human" macroecosystem.

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## **Conflict of interests**

The authors declare that they have no conflicts of interest.

## **Ethical Approval**

Non-applicable.

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Conceptualization, A.V.L., L.V.O., V.I.P. and N.M.T.; Data curation, A.V.L., L.V.O., V.I.P., N.M.T. and A.S.S.; Investigation, A.V.L., L.V.O., V.I.P., N.M.T., A.S.S., E.A.Z., K.A.K. and D.V.A.; Supervision, A.V.L. and L.V.O.; Validation, V.I.P., N.M.T., A.S.S., E.A.Z., K.A.K. and D.V.A.; Roles/Writing - original draft, E.A.Z., K.A.K. and D.V.A.; Writing - review & editing, A.V.L., L.V.O., V.I.P., N.M.T. and A.S.S.

## 6. References

Berg, G.; Grube, M.; Schloter, M. and Smalla, K. (2014). Unraveling the plant microbiome: looking back and future perspectives. Frontiers in microbiology. 5: 148. https://doi.org/10.3389/fmicb.2014.00148.

Bhattacharjee, P.; Karim, K.A. and Khan, Z. (2023). Harnessing the Microbiome: A Comprehensive Review on Advancing Therapeutic Strategies for Rheumatic Diseases. Cureus. 15(12): e50964. https://doi.org/10.7759/cureus.50964.

Blum, W.E.H.; Zechmeister-Boltenstern, S. and Keiblinger, K.M. (2019). Does Soil Contribute to the Human Gut Microbiome?. Microorganisms. 7(9): 287. https://doi.org/10.3390/microorganisms7090287.

**Blum, H.E. (2017).** The microbiome: A key player in human health and disease. Journal of Healthcare Communications. 2: 1–5. https://doi.org/10.4172/2472-1654.100062.

Brown, M.D.; Shinn, L.M.; Reeser, G.; Browning, M.; Schwingel, A.; Khan, N.A. et al. (2022). Fecal and soil microbiota composition of gardening and non-gardening families. Scientific Reports. 12(1): 1595. <u>https://doi.org/10.1038/s41598-022-05387-5</u>.

**Bu, S.; Beavers, A.W.; Sugino, K.Y.; Keller, S.F.; Alaimo, K. and Comstock, S.S. (2024).** Influence of Compost Amendments on Soil and Human Gastrointestinal Bacterial Communities during a Single Gardening Season. Microorganisms. 12(5): 928.

https://doi.org/10.3390/microorganisms12050928.

Carabotti, M.; Scirocco, A.; Maselli, M.A. and Severi, C. (2015). The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. Annals of Gastroenterology. 28(2): 203-209.

**Destoumieux-Garzón, D.; Mavingui, P.; Boetsch, G.; Boissier, J.; Darriet, F.; Duboz, P. et al. (2018).** The One Health Concept: 10 Years Old and a Long Road Ahead. Frontiers in Veterinary Science. 5: 14. https://doi.org/10.3389/fvets.2018.00014.

**Divangahi, M.; Khan, N. and Kaufmann, E. (2018).** Beyond Killing *Mycobacterium tuberculosis*: Disease Tolerance. Frontiers in Immunology. 9: 2976. https://doi.org/10.3389/fimmu.2018.02976.

**Donal, P.F.; Gree, R.E. and Heath, M.F. (2001).** Agricultural intensification and the collapse of Europe's farmland bird populations. Proceedings of Biological Sciences. 268(1462): 25-29. https://doi.org/10.1098/rspb.2000.1325.

Edwards, V.; Smith, D.L.; Meylan, F.; Tiffany, L.; Poncet, S.; Wu, W.W. et al. (2021). Analyzing the Role of Gut Microbiota on the Onset of Autoimmune Diseases Using  $TNF^{\Delta ARE}$  Murine Model. Microorganisms. 10(1): 73. https://doi.org/10.3390/microorganisms10010073.

Erdman, S.E. and Poutahidis, T. (2017). Gut microbiota modulate host immune cells in cancer development and growth. Free Radical Biology & Medicine. 105: 28–34. https://doi.org/10.1016/j.freeradbiomed.2016.11.013.

Flandroy, L.; Poutahidis, T.; Berg, G.; Clarke, G.; Dao, M.C.; Decaestecker, E. et al. (2018). The impact of human activities and lifestyles on the interlinked microbiota and health of humans and of ecosystems. The Science of the Total Environment. 627: 1018-1038.

https://doi.org/10.1016/j.scitotenv.2018.01.288.

Gilbert, J.A.; Blaser, M.J.; Caporaso, JG.; Jansson, J.K.; Lynch, S.V. and Knight, R. (2018). Current understanding of the human microbiome. Nature Medicine. 24(4): 392-400. https://doi.org/10.1038/nm.4517.

Gupta, A.; Gupta, R. and Singh, R.L. (2016). Microbes and Environment. Principles and Applications of Environmental Biotechnology for a Sustainable Future. 15: 43-84. https://doi.org/10.1007/978-981-10-1866-4\_3.

**Hirt, H. (2020).** Healthy soils for healthy plants for healthy humans: How beneficial microbes in the soil, food and gut are interconnected and how agriculture can contribute to human health. EMBO Reports. 21(8): e51069.

https://doi.org/10.15252/embr.202051069.

Jang, H.J.; Lee, N.K. and Paik, H.D. (2024). A Narrative Review on the Advance of Probiotics to Metabiotics. Journal of Microbiology and Biotechnology. 34(3): 487-494. https://doi.org/10.4014/jmb.2311.11023.

Khan, M.F. and Wang, H. (2020). Environmental Exposures and Autoimmune Diseases: Contribution of Gut Microbiome. Frontiers in Immunology. 10: 3094. https://doi.org/10.3389/fimmu.2019.03094. Kirjavainen, P.V.; Karvonen, A.M.; Adams, R.I.; Täubel, M.; Roponen, M.; Tuoresmäki, P. et al. (2019). Farm-like indoor microbiota in non-farm homes protects children from asthma development. Nature Medicine. 25(7): 1089-1095. https://doi.org/10.1038/s41591-019-0469-4.

Kurilshikov, A.; Wijmenga, C.; Fu, J. and Zhernakova, A. (2017). Host Genetics and Gut Microbiome: Challenges and Perspectives. Trends in Immunology. 38(9): 633–647. https://doi.org/10.1016/j.it.2017.06.003.

Lahlali, R.; Ezrari, S.; Radouane, N.; Kenfaoui, J.; Esmaeel, Q.; El Hamss, H. et al. (2022). Biological Control of Plant Pathogens: A Global Perspective. Microorganisms. 10(3): 596. https://doi.org/10.3390/microorganisms10030596.

Liao, H.; Li, X.; Yang, Q.; Bai, Y.; Cui, P.; Wen, C. et al. (2021). Herbicide Selection Promotes Antibiotic Resistance in Soil Microbiomes. Molecular Bbiology and Evolution. 38(6): 2337–2350. https://doi.org/10.1093/molbev/msab029.

Liu, Z.; Cao, S.; Sun, Z.; Wang, H.; Qu, S.; Lei, N. et al. (2021). Tillage effects on soil properties and crop yield after land reclamation. Scientific Reports. 11(1): 4611. <u>https://doi.org/10.1038/s41598-021-84191-z</u>.

Lorenzetti, L.A. and Fiorini, A. (2024). Conservation Agriculture Impacts on Economic Profitability and Environmental Performance of Agroecosystems. Environmental Management. 3: 532-545. <u>https://doi.org/10.1007/s00267-023-01874-1</u>.

Manyi-Loh, C.; Mamphweli, S.; Meyer, E. and Okoh, A. (2018). Antibiotic Use in Agriculture and Its Consequential Resistance in Environmental Sources: Potential Public Health Implications. Molecules. 23(4): 795. https://doi.org/10.3390/molecules23040795.

Matute, P.S. and Iyavoo, S. (2023). Exploring the gut microbiota: lifestyle choices, disease associations,

and personal genomics. Frontiers in Nutrition. 10: 1225120. <u>https://doi.org/10.3389/fnut.2023.1225120</u>.

Meena, R.S.; Kumar, S.; Datta, R.; Lal, R.; Vijayakumar, V.; Brtnický, M. et al. (2020). Impact of agrochemicals on soil microbiota and management: a review. Land. 9: 34. https://doi.org/10.3390/land9020034.

Mendes, R. and Raaijmakers, J.M. (2015). Crosskingdom similarities in microbiome functions. The ISME Journal. 9(9): 1905-1907. https://doi.org/10.1038/ismej.2015.7.

Panthee, B.; Gyawali, S.; Panthee, P. and Techato,K. (2022). Environmental and Human Microbiome forHealth.Life.Life.12(3):https://doi.org/10.3390/life12030456.

Pantigoso, H.A.; Newberger, D. and Vivanco, J.M. (2022). The rhizosphere microbiome: Plant-microbial interactions for resource acquisition. Journal of Applied Microbiology. 133(5): 2864-2876. https://doi.org/10.1111/jam.15686.

Postler, T.S. and Ghosh, S. (2017). Understandingthe Holobiont: How Microbial Metabolites AffectHuman Health and Shape the Immune System. CellMetabolism.26(1):110-130.https://doi.org/10.1016/j.cmet.2017.05.008.

Reber, S.O.; Siebler, P.H.; Donner, N.C.; Morton, J.T.; Smith, DG.; Kopelman, J.M. et al. (2016). Immunization with a heat-killed preparation of the environmental bacterium *Mycobacterium vaccae* promotes stress resilience in mice. Proceedings of the National Academy of Sciences of the United States of America. 113(22): E3130–E3139. https://doi.org/10.1073/pnas.1600324113.

Rothschild, D.; Weissbrod, O.; Barkan, E.; Kurilshikov, A.; Korem, T.; Zeevi, D. et al. (2018). Environment dominates over host genetics in shaping human gut microbiota. Nature. 555(7695): 210-215. https://doi.org/10.1038/nature25973. Rowland, I.; Gibson, G.; Heinken, A.; Scott, K.; Swann, J.; Thiele, I. et al. (2018). Gut microbiota functions: metabolism of nutrients and other food components. European Journal of Nutrition. 57(1): 1-24. https://doi.org/10.1007/s00394-017-1445-8.

Rowson, M.; Jolly, M.; Dickson, S.; Gifford, M.L. and Carré, I. (2024). Timely symbiosis: circadian control of legume-rhizobia symbiosis. Biochemical Society Transactions. 52(3): 1419-1430. https://doi.org/10.1042/BST20231307.

Samaddar, S.; Karp, D.S.; Schmidt, R.; Devarajan, N.; McGarvey, J.A.; Pires, A.F.A. et al.. (2021). Role of soil in the regulation of human and plant pathogens: soils' contributions to people. Philosophical Transactions of the Royal Society of London. 376(1834): 20200179. https://doi.org/10.1098/rstb.2020.0179.

Schuijs, M.J.; Willart, M.A.; Vergote, K.; Gras, D.; Deswarte, K.; Ege, M.J. et al. (2015). Farm dust and endotoxin protect against allergy through A20 induction in lung epithelial cells. Science. 349(6252): 1106-1110. <u>https://doi.org/10.1126/science.aac6623</u>.

Tanaka, M.; Kohchi, C.; Inagawa, H.; Ikemoto, T. and Hara-Chikuma, M. (2022). Effect of topical application of lipopolysaccharide on contact hypersensitivity. Biochemical and **Biophysical** Communications. 586: 100-106. Research https://doi.org/10.1016/j.bbrc.2021.11.045.

van Bruggen, A.H.C.; Goss, E.M.; Havelaar, A.; van Diepeningen, A.D.; Finckh, M.R. and Morris, J.G.Jr. (2019). One Health - Cycling of diverse microbial communities as a connecting force for soil, plant, animal, human and ecosystem health. Science of the Total Environment. 664: 927-937. https://doi.org/10.1016/j.scitotenv.2019.02.091.

Wagner, M.R.; Lundberg, D.S.; Del Rio, T.G.; Tringe, S.G.; Dangl, J.L. and Mitchell-Olds, T. (2016). Host genotype and age shape the leaf and root microbiomes of a wild perennial plant. Nature Communications. 7: 12151. https://doi.org/10.1038/ncomms12151.

Wicaksono, W.A.; Cernava, T.; Wassermann, B.; Abdelfattah, A.; Soto-Giron, M.J.; Toledo, G.V. et al. (2023). The edible plant microbiome: evidence for the occurrence of fruit and vegetable bacteria in the human gut. Gut Microbes. 15(2): 2258565. https://doi.org/10.1080/19490976.2023.2258565.

Wittwer, R.A.; Bender, S.F.; Hartman, K.; Hydbom, S.; Lima, R.A.A.; Loaiza, V. et al. (2021). Organic and conservation agriculture promote ecosystem multifunctionality. Science Advances. 7(34): eabg6995. https://doi.org/10.1126/sciady.abg6995.

Zhang, W.; Li, J.; Zhang, Y.; Wu, X.; Zhou, Z.;

**Huang, Y. et al. (2022).** Characterization of a novel glyphosate-degrading bacterial species, *Chryseobacterium* sp. Y16C, and evaluation of its effects on microbial communities in glyphosate-contaminated soil. Journal of Hazardous Materials. 432: 128689.

https://doi.org/10.1016/j.jhazmat.2022.128689.

Zhang, L.; Chu, J.; Hao, W.; Zhang, J.; Li, H.; Yang, C. et al. (2021). Gut Microbiota and Type 2 Diabetes Mellitus: Association, Mechanism, and Translational Applications. Mediators of Inflammation. 2021: 5110276. https://doi.org/10.1155/2021/5110276.

Zhou, D.; Li, N.; Yang, F.; Zhang, H.; Bai, Z.; Dong, Y. et al. (2022). Soil causes gut microbiota to flourish and total serum IgE levels to decrease in mice. Environmental Microbiology. 24(9): 3898-3911. https://doi.org/10.1111/1462-2920.15979.

Zhou, D.; Zhang, H.; Bai, Z.; Zhang, A.; Bai, F.; Luo, X. et al. (2016). Exposure to soil, house dust and decaying plants increases gut microbial diversity and decreases serum immunoglobulin E levels in BALB/c mice. Environmental Microbiology. 18(5): 1326-1337. https://doi.org/10.1111/1462-2920.12895.