Distortion of the Microbiota of the Natural Environment by Human Activities

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Abstract Natural environmental microbiota is extremely abundant and diverse in environments traditionally occupied by humans. Humans, like other animals, cause shifts in the microbiota in their living environment. The exceptional scale and longevity of these shifts pose a risk to natural and seminatural ecosystems and human health. Environmental pollution, non-native invasive plant species, and vegetation control by humans distort seasonal fluctuation and directly alter natural microbiota. They also reduce the accessibility of natural environmental microbiota in urbanized societies. The removal of organic surface soil and its substitution with man-made surfaces is the most extreme example of the distortion of natural microbiota; it cuts the number of microbial cells per gram soil to one thousandth or one hundred thousandth of the original level. Since humans evolved in continuous contact with environmental microbiota, efforts to rewild urban microbiota are being developed to reintroduce diverse contacts with microbiota of the natural environment to everyday life of urban dwellers. Recent findings suggest that these efforts may lead to enhanced immune modulation. Further research is needed to understand whether this eventually results in a lower incidence of immune-mediated diseases in urbanized societies.

Keywords Environmental microbiota · Biodiversity · Built environment · Dirt · Green infrastructure · Immune response · Plant invasions · Pollution · Urban rewilding · Vegetation control

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1 Natural Environmental Microbiota

1.1 Environmental Microbes Are Ubiquitous

Microbes are ubiquitous and extremely abundant in natural environments. A tiny gram of organic surface soil typically contains one to ten billion bacterial 16S rRNA gene sequences [1]; millions to billions of viruses, including bacteriophages and plant viruses; Archaea; fungal cells; algae; and hundreds to thousands of microscopic multicellular Eukaryotes, like soil animals [2–4]. The exact taxonomic composition of the soil microbiome ranges considerably at all spatial scales, from large-scale variation between geographic regions to differences between nearby field plots within a single forest stand and even between neighboring soil samples at the centimeter scale [5–7]. In the so far largest meta-analysis to map Earth's bacteriome, the predicted average gene copy number of a bacterial strain was less than ten per 1 g soil [6]. In the same study, bacterial 16S rRNA gene copies in plant rhizosphere were slightly more abundant compared to bulk soil samples. Although the number of 16S rRNA gene copies per sample can be ten times lower on plant leaves than in soil [6], microbes occupy virtually every organic surface on Earth. Providing that environmental conditions are not too dry, cold, hot, or toxic, biofilms, i.e., surface-attached clusters of bacteria, often cover inorganic soil particles and bedrock as well [8].

1.2 Patterns in Natural Microbial Diversity

According to current understanding, the taxonomic diversity and the abundance of natural microbial communities tend to follow certain general patterns. At the global scale, Thompson et al. [6] found evidence that low latitudes have richer soil and plant bacterial communities compared to higher latitudes, a pattern known to exist among multicellular organisms, including plants and most fungi [4, 9]. Recent studies indicate a second general pattern: the overall microbial diversity seems to decline with soil depth. Liang et al. [2] sampled agricultural red clay soils from the depth 0–120 cm in Alabama and observed that the diversity of bacterial communities and the abundance of viruses decreased with increasing sampling depth. They also observed an association between viruslike particles and bacterial diversity. Upton et al. [10] observed that grassland fungal diversity declines with soil depth, the richness being 50% lower between 60 and 100 cm than between 0 and 10 cm below soil surface.

The third pattern is related to the utilization of resources: although microbial diversity and the abundance of different taxa vary considerably within small spatial scales, Spain et al. [11] stated *Proteobacteria* to be the dominant phylum in surface soils in a study that included samples from natural tall prairie soils and data from earlier studies covering different continents and ecosystems [12]. The high abundance of soil *Proteobacteria* seems to be limited to the uppermost soil layers where

plant-based organic material is degraded and where the microbial co-occurrence network is complex [11]. As the majority of soil bacteria are still unclassified [6], it is unsure whether the phylum *Proteobacteria* will retain its position as the most common phylum in surface soils. Despite this, the high abundance of *Proteobacteria* in natural surface soils is a fact that may have played a role in human evolution (see other chapters in this book).

While soil microbial diversity seems to follow certain relatively universal patterns, the factors modulating microbial diversity on and inside plant leaves are complex. Experimental evidence suggests that the main determinants of leaf bacterial diversity and community structure are the host species and its functional traits, such as leaf mass per area, leaf longevity and maximum photosynthetic capacity, leaf nitrogen content, and wood density [13]. In a field study, fungal assemblages on beech (*Fagus sylvatica*) leaves were largely dominated by cosmopolitan and generalist species, and the largest variation was found between individual leaves within the same canopy [14]. Between trees, the major determinant of community dissimilarities was tree genotype, instead of geographical distance [14]. In addition, leaf mineral content has been found to be crucial for leaf microbial community composition [15]. Since fertilization, irrigation, and urbanization affect nitrogen availability, natural microbial communities of plant leaves are governed by several factors that are modified and even distorted by humans.

1.3 Seasonal Variation in Natural Microbial Communities

Complex interactions between soil abiotic conditions, like temperature, frost, moisture, porosity, and biotic factors, such as the composition and coverage of vegetation, affect microbial community structure and activity in natural soils. Drought during dry seasons distorts soil invertebrate communities [16] and halts microbial respiration when microscale hydrologic connectivity is poor [17]. Seasonal variation, particularly permanent snow cover, narrows the options humans have to interact with natural microbial communities.

In Mediterranean and warmer climates, the cycling between dry and rainy seasons shapes microbial activity and phylogenetic diversity in natural surface soils [17, 18]. In temperate and boreal climates, fall colors, leaf fall, and the subsequent litter decay are the brightest example of seasonal variation in native plant and microbial communities [19–22]. As seasonal variation does not destroy natural microbial communities but instead is an essential part of most ecosystems on Earth, humans must have adapted to seasonal changes in microbial environment. Thus, the importance of seasonal variation in the context of immune system function is limited to cases where a hostile season, like winter, reduces contacts with environmental microbiota [23].

1.4   Environmental Bacteria Are Lazy Survivors

One of the greatest challenges in environmental microbial ecology has been to understand why microbial activity in surface soils does not rapidly metabolize and recycle all organic carbon that enters soil ecosystems [24, 25]. Recent experimental and modelling approaches have offered at least two complementary scenarios. Firstly, as large biofilms, e.g., clusters of bacteria, may partly prevent the flow of resources in microscopic pores, competition in porous media seems to favor steadily slow-growing biofilm-forming bacteria over fast-growing strains [25]. In parallel, decomposers need to produce extracellular enzymes to utilize organic carbon sources [24]. The resources released by extracellular enzymes can be exploited by any non-decomposing coexisting species; recent findings indicate that the presence of the free riders increases organic matter buildup and bacterial biomass in surface soils [24]. Owing to these two phenomena and the functional complexity of soil organic carbon [26], a successful strategy in natural surface soils is opportunistic laziness. Notably, in addition to soils, many other organic surfaces, such as plant leaves and human skin, can be regarded as partially porous systems where the utilization of resources requires the release of extracellular enzymes. The inevitable conclusion is that humans evolved in the overwhelming presence of lazy microbial survivors that arrive on the skin and mucous membranes in billions each day.

1.5   Lazy Survivors and Modern Medicine

The opportunistic laziness is in striking contrast with the tradition of studying microbes in medical sciences. The modern success of medicine is based on Koch's postulates [27]. The postulates require (1) that a pathogen is distinguished in each patient; (2) that the pathogen, e.g., a bacterial species, is isolated from the host with the disease; and (3) that it is grown in pure culture. Finally, (4) the disease should be reproduced by inserting the cultured pathogen into a healthy host. Koch's postulates are followed also in the prevention of diseases, but in a reverse order. To pass the postulates, the cure, e.g., a probiotic bacterial strain, must be (1) exactly identified and (2) found in former patient, and (3) the strain has to heal new patients. As the human immune system coevolved to continuously cope with an extremely diverse, seasonally and locally changing network of lazy survivors, the characteristics required by Koch's postulates are hardly found in environmental microbiota. In the context of the hygiene hypothesis, if the postulates are followed, over 99% of environmental bacteria drop out simply because they cannot be cultivated. This is unfortunate as recent findings indicate that the whole spectrum of environmental microbiota may be needed for optimal prevention of immune-mediated diseases [28].

2 Man-Made Variation in Environmental Microbiota

2.1 Many Species Shape the Microbiota of Their Surroundings

Humans are not the only species whose activity results in considerable alteration in microbial communities. Tree-fungal interactions largely control microbial environment and are indeed the key to ecosystem productivity in large parts of the world [29]. Many animals, like ants and large herbivores, drastically affect the microbiota in their surroundings [30, 31]. Just like humans, several vertebrates clean their nests to reduce microbial load on the offspring. Termites build mounds and form large colonies where the number of individuals is comparable to human cities. In the mounds, microbial diversity and the seasonal variation of community composition are smaller than in surrounding soils [32]. The main difference between humans and other species is the scale: when cultural evolution proceeded in humans, our species became the first one that is able wipe off natural vegetation and substitute natural ground surface with artificial materials that lack coevolved microbial communities.

2.2 Invasive Species

Invasive species distort native microbial communities and are one of the major reasons for biodiversity decline on this planet. Humans typically control, e.g., weed and substitute, native vegetation in urban environments, which results in low plant diversity. The poor diversity and the short evolutionary history of urban plant communities leave the door open for successful invasion by exotic plant species [33, 34]. Outside developed societies, invasive species destroy entire ecosystems utilized by locals [35]. An example can be found from coastal South-East Asia where sand dunes host a diverse community of native woody species [36, 37]. Many of these plants have traditionally belonged to the local diet [38]. When the native plant community on nutrient-poor sand dunes is invaded and replaced by alien nitrogen-fixing acacias (Fig. 1), the entire lifestyle of locals is under threat, including the fiber- and microbe-rich traditional diet.

Mechanisms behind plant invasiveness are numerous [39]. In the context of soil microbiota, many invasive species release compounds or produce litter that either slows down or accelerates litter decomposition by soil microorganisms [39–42]. This often leads to poor regeneration of native vegetation [39, 43, 44], which plausibly results in shifts in microbial community composition. Some of the mechanisms of the distortion of natural microbial communities are complex; within introduced range, legumes are known to host root symbionts that produce compounds that bind micronutrients [45–47]. As a result of micronutrient binding, soil dominated by invasive garden lupine (Fig. 1; [48], see also Vetter et al. [49]) contains less nematode root feeders than soil dominated by a native legume

Fig. 1 Two examples on how invasive species distort soil natural microbial communities. (**a**) In temporal and boreal Europe, root symbionts of North American garden lupine (*Lupinus polyphyllus*) reduce the abundance of root feeders, which leads to monocultures that shine in early summer and are thereafter less attractive for human recreation. (**b**) In South-East Asia, native dune forests host a diverse plant community adapted to flourish on nutrient-poor sand, but fast-growing Australian acacia grows successfully on the dunes. The pictured, mature tree is 6 years old. (**c**) Acacia litter forms a suitable habitat for acacia seedlings. (**d**) The root system of acacia includes a network of nitrogen-fixing root nodules in the uppermost sand layer, which leads to the distortion of the microbiota of the natural environment and aids in replacement of native vegetation. (Photos taken by the author)

[46]. As root feeding by nematodes reduces plant growth and reproduction [50], the decreased herbivory (i.e., decreased feeding on plants by the nematode root feeders) then provides a competitive advantage for the legume over native plants. This advances the invasion and distorts the original microbial community in surface soil [51]. In addition to direct effects on soil microbiota, invasive plants may reduce the attractiveness of nearby natural and semiwild areas. In Europe, lupine invasion is often accompanied by native but sticky nettles that benefit from the increased nutrient content of lupine-dominated soils. As a result, the recreational value and possibilities for direct contacts with rich microbiota in green areas are diminished.

In well-replicated field experiments, exotic plant species have increased above-ground microbial diversity as a part of diverse plant communities [13, 52]. Despite this, monocultures of alien plants simplify molecular diversity of organic compounds in soil [26]. This is crucial as according to recent models, molecular diversity controls decomposition and thus eventually litter formation [26]. To put it shortly, cumulative evidence supports the view that invasive alien species distort natural microbial communities and the interaction of humans with the surrounding nature.

2.3 Environmental Pollution

Environmental pollution occurs virtually everywhere where human population density is high. In the context of natural microbial communities, contaminants can be divided into organic compounds and elemental contaminants. Nutrients released by human societies often act like organic contaminants [53]. Elemental contaminants are nondegradable, but they may be extracted by plants, bound to organic molecules, and their toxicity can be adjusted by manipulating solubility [54, 55]. While organic contaminants can be recalcitrant, they are usually degradable. Whether or not they are degraded depends on the contaminant and the local microbial community, like the presence of degrader genes [56, 57]. If nutrient availability or oxygen content is low, degradation is delayed [58]. This can be corrected by adding nutrients, which further distorts the original microbial community [59, 60]. The most common organic contaminants are aliphatic and polyaromatic hydrocarbons, pesticides, and chlorinated compounds. All these typically serve as a carbon and sometimes also nitrogen source for indigenous soil microbes. The utilization of a novel carbon or energy source obviously causes shifts in microbial community composition. The distortion changes the abundance and diversity of bacteria associated with human health, particularly immune system disorders [61, 62].

As the release of environmental contaminants has been a part of industrialized, urbanized lifestyle from the very beginning, low contaminant levels are found in urban surface soils [63]. Even low contaminant levels have the potential to distort plant and microbial growth [63–66]. Although some of the most common organic pollutants, like oil hydrocarbons, are often degraded rapidly in nature, the lack of organic topsoil prolongs the time needed for degradation [67, 68]. In urban areas, organic topsoil is regularly removed (see below). Recently, low levels of polyaromatic hydrocarbons in ambient air were observed to be associated with the high endocrine disruption potential of individual gut microbial communities among daycare children [69]. While the method used does not allow conclusions about a causal effect, earlier experimental work with cell models supports the finding by Roslund et al. [69–72]. Later, Vari et al. [73] found a similar but inverse association between the endocrine disruption potential of the gut microbial community and the coverage of broadleaved and mixed forests in urban environment. These findings support the view that environmental pollution causes functional shifts in microbial communities. More detailed studies are needed to confirm or reject the hypothesis about the connection between endocrine disruption potential of the gut metagenome and environmental pollution in urban areas.

In summary, environmental pollution has been shown to change environmental and commensal microbial community composition, and there is indirect evidence that the microbial changes are related to health, including immune-mediated diseases.

2.4   Vegetation Control and the Network of Lazy Survivors

In developed countries, rural areas are largely utilized for agriculture and forestry. The resulting land use changes are a threat to biodiversity. In the context of environmental microbial communities, monocultures have different and often poorer microbial networks compared to diverse vegetation [74, 75]. Interestingly, some monocultures decrease the relative abundance of *Proteobacteria* [74]. From the perspective of immune modulation, however, the traditional agricultural lifestyle (Fig. 2) evidently provides protection against allergic disorders [76]. Compared to agricultural and forestry systems that are characterized by rich weed populations and abundant patches of pristine and idle land, vegetation control can be extreme in urban areas. At least the following practices have a major impact on the composition, function, dynamics, and diversity of microbial communities in urban areas:

1. Removal of organic surface soil and plant debris (Fig. 2). In rural areas, plant litter is typically left aside. In urban green spaces, dead plant parts, stumps, fallen

Fig. 2 Distortion of natural microbiota in urban areas. Upper row: Urban playgrounds and other built environment comprising of man-made surfaces have poor possibilities for physical contact with rich environmental microbiota. In traditional agricultural societies (below), lifestyle-facilitated unintentional, rich, and daily contacts with environmental microbiota. Left: Farmer's child in front of cattle and hut in Kenya. Right: Under the Yoke (Burning the Brushwood) by Eero Järnefelt (1893). Birch forest burning for agricultural fields. (Photos by the author except painting: Finnish National Gallery/Yehia Eweis. Creative commons CCO)

autumn leaves, and even thatch are systemically removed. This disturbs the nutrient cycle, eradicates niches suitable for decomposers, and affects water retention on the soil surface. In nongreen urban space, artificial surface materials, like asphalt, concrete, and buildings, prevail. When these surfaces are built, the native microbial community, the rich network of lazy survivors, is removed. The complete elimination of the original microbiota, combined with poor abundance of environmental microbiota on the artificial surfaces, is one of the main reasons for poor microbial exposure among urbanites [77, 78].

2. Intensive fertilization and irrigation. While agricultural fields are regularly treated with nitrogen-fixing legumes or slowly soluble or mineral fertilizers, the rest is usually left outside severe disturbance in rural areas. In contrast, most urban lawns and ornamentals receive intensive fertilization and—depending on climate—irrigation to meet recreational needs [79, 80]. Since fertilization and natural variation in soil moisture are crucial determinants of microbial community composition, the man-made modification of urban soils will evidently distort natural microbial communities [81].

3. Removal of dust particles from city centers. In nature, wind blows dust and tiny organic particles to nearby rocky and otherwise bare patches. Little by little, this leads to accumulation of organic matter suitable for plant and microbial growth. In urban areas, streets, sidewalks, cycle paths, and city centers are cleaned, brushed, and even washed to keep dirt away. As dirt-free mineral soils and artificial surfaces have low microbial abundance [3, 82, 83], dirt removal severely limits the network of lazy survivors, i.e., environmental microbial communities in urban areas. The low abundance and likely patchiness of urban environmental microbiota is reflected on skin microbiota of urban dwellers: in a study by Grönroos et al. [84], touching organic gardening soils or moss for less than a minute multiplied the number of 16S rRNA gene sequences on the skin of urban volunteers, even though bacterial abundance was measured after washing hands with tap water.

4. Green space design. Touching is beneficial for efficient transfer of environmental microbiota onto the skin and mucosal membranes [83–86]. Typical urban public green spaces, parks, and playgrounds do not particularly encourage physical contact with organic soil, herbs, perennials, and woody plants. On the contrary, greenery is typically a decorative element that promotes recreation but discourages active interaction, like touching and tasting (Fig. 3). Related to this, high durability is a main target in playground design. Because natural materials wear out, artificial materials like gum crumb, asphalt, concrete, gravel, and sand are preferred (Fig. 2). All these are hostile environments for most environmental microbes, which keep the microbial network of lazy survivors out of reach of many urban children.

5. City design. Most cities were largely planned before urban principles for ecological landscape design were thought about [88]. Nowadays, new evidence supporting the link between immune-mediated diseases and urban land cover is being published regularly (see [23, 89]). This new knowledge has not yet been fully considered in urban planning, e.g., in the placement of small green spaces

Fig. 3 Upper left: Urban green is often for decoration, not for active interaction. Combined with dirt removal from city centers and sidewalks, intentional rewilding of urban areas is needed. Lower left: A hole in multispecies lawn hosts a rich network of environmental microbiota and attracts skin contact. Lower middle: Woody plant parts, like sticks, provide close contact with environmental microbiota in winter. Right: High-biodiversity green space has diverse vegetation [77] and dead wood [87], and it encourages engaging with natural elements [3]. (Figures by the author, except: Right permission by Maria Hyvönen)

that enrich nearby microbial communities and allow abundant contacts with natural microbiota.

Taken together, two parallel phenomena affect to the same direction in urban areas. These are the rare contacts with rich sources of environmental microbiota in urban green areas and the reduction of natural microbial abundance and diversity within built areas per se. The five factors mentioned above lead to severe distortion of ground surface microbiota in urban centers and neighborhoods, which according to Parajuli et al. [90] limit contacts with diverse and abundant environmental microbiota also indoors. In detail, Parajuli et al. [90] studied standardized doormats that were kept in rural and urban households for 2 weeks and analyzed doormat bacterial communities. The results revealed that the high coverage of built environment reduces the transfer of environmental microbial communities indoors. Later, the reduced transfer was found to exist in both summertime and winter samples [91]. Alarmingly, the authors also realized that the winter minimum in rural areas was at the same level as the summer maximum within urban, heavily built neighborhoods [91]. Later, Parajuli et al. [77] realized that low yard vegetation diversity is associated with dysbiosis in stool microbiota among urban dwellers. The distortion of microbiota within built areas has been observed in indoor dust and air samples as well [92–94]. The conclusion is that environmental microbiota, the rich network of lazy survivors that humans coevolved with, is deprived in urban settings, which severely distorts and limits microbial exposure among urbanites.

3   Biodiversity Intervention, i.e., How to Cure the Consequences of the Distortion

3.1   Why Bother?

Changes in land use typically lead to biodiversity loss. Hanski et al. [89] were the first to find that the high coverage of built environment is related to immune-mediated diseases. Recently, Nurminen et al. [23] found that a high coverage of built environment next to infant's homes increases the probability of type 1 diabetes among genetically vulnerable individuals. As an opposite, the abundance of agricultural environment—comprising nonirrigated arable land, fruit trees and berry plantations, pastures, natural pastures, land principally occupied by agriculture with significant areas of natural vegetation, and agroforestry areas—was inversely associated with the probability of the disease. The study by Nurminen et al. [23] took place in three hospital districts in Finland. When the districts were analyzed separately, the inverse association of the agricultural environment with type 1 diabetes was found to be pronounced in the southernmost study district. The annual snow-free period decreases from north to south in Finland. Nurminen et al. [23] collected doormat debris to study seasonal variation in biodiversity carried inside by families participating in the study. The results revealed that indoor exposure to environmental biodiversity was low when snow covers the ground, compared to snowless samples. The authors explain that when snow covers the ground for several months, the benefits of high microbial diversity in the agricultural environment cannot be accessed as easily and unintentionally as during the rest of the year. When the results by Nurminen et al. [23] are considered in the context of intentionally increasing exposure to biodiversity among urbanites, any potential solutions should consider winter and other natural factors that may prevent contacts with microbially diverse soil and vegetation. In warmer regions, seasonal patterns in precipitation need to be considered when planning biodiversity interventions and urban rewilding.

3.2   Outdoor Vegetation Interventions

While the global network of protected areas has been built to cover natural and seminatural ecosystems [95], the need to protect and rewild urban ecosystems has been recognized recently [96]. In addition to the global network of the most valuable natural ecosystems, the biodiversity in urban forests in some countries is increasing due to modern management practices, e.g., saving dead wood [87]. As a striking contrast, dominant management practices in parks and small green spaces inside built areas result in low exposure to biodiversity among urban dwellers (see Sect. 2.3. and [83, 90]). Since the low exposure to rich environmental microbiota within built areas is often accompanied with a lifestyle that actively or passively avoids visits to forests and other natural and seminatural areas, only nature-oriented

urbanites are likely to receive the benefit of the rich microbial network of lazy survivors that lurks in dirt of urban nature in developed countries [97–99]. Since efforts to change human behavior typically have limited value, there is a good reason to concentrate on the opposite approach, i.e., biodiversity interventions within built areas [78]. These would rewild urban ecosystems by adding biodiversity to areas where urbanites usually spend time in their everyday lives.

Roslund et al. [78] were the first to test if the transfer of green elements known to contain rich and abundant environmental microbial communities affects immune modulation among urban dwellers. They selected daycare children aged 3–5 years as the target group. Three types of daycare centers were included: the so-called nature daycare centers where children spend time in nearby forests on a daily basis, regular urban daycare centers that have a yard dominated by artificial and mineral soil materials, and the so-called intervention daycare centers that received green yards overnight. The intervention daycare centers were randomly selected from the participating regular urban daycare centers. Intervention materials consisted of readily vegetated, boreal forest floor; sod, i.e., transferable lawn; peat blocks; and planting boxes that daycare personnel were advised to fill with microbially rich gardening soil, instead of bulk gardening soil that is a microbially poor mixture of peat, sand, and fertilizers. The intervention lasted for 4 weeks, and the children were actively guided to be in contact with the green materials on a daily basis, 5 days a week. Since children were fascinated by the green elements, the guidance was not as crucial as originally assumed [3]. Skin swabs and stool and blood samples were collected before the intervention and after it on Day 28. The results showed that skin microbiota among the intervention children shifted during the intervention and became similar with skin microbiota among children in nature daycare centers. The shifts were particularly evident within proteobacterial classes *Alpha-* and *Gammaproteobacteria*. These shifts were associated with enhanced immune regulation [78].

The study by Roslund et al. [78] had a relatively small sample size of altogether 75 children. The sampling size was further limited due to unwillingness of study participants to donate blood. A parallel difficulty was to keep the interest of families participating in the trial at standard daycare centers without the green intervention. Ideally, the study by Roslund et al. [78] will be repeated as a randomized block design with the participation of tens of daycare centers and hundreds of children that would be followed for years to understand potential effects on disease incidence. Despite these difficulties, the work by Roslund and collaborators paved the way for intervention trials that will be needed to reach a sound basis for microbially oriented rewilding of urban neighborhoods.

Hui et al. [83] described an alternative strategy for rewilding the urban microbiome, i.e., enriching mineral soils with biologically rich, standardized dirt. The authors allowed volunteers to touch pure commercial sand materials or the same materials mixed with biodiverse dirt. The results showed how skin biodiversity increased in dirt-enriched sand. The authors monitored how the dirt intervention affected the relative abundance of bacterial genera containing opportunistic pathogens on the skin [83]. They concluded touching dirt that contains the rich network of

lazy environmental microbiota does decrease the relative abundance of genera containing opportunistic pathogens on the skin, compared to touching pure sand materials. An interesting revelation was that touching any soil decreased the relative abundance of the genera containing opportunistic pathogens, compared to samples taken before the intervention started [83].

Today, city-level, regional, and even national practices and guidelines have been created to advance urban greening. Children are usually a special target group in those guidelines. Preference for wooden jungle gyms and other playground structures, use of sod, and urban revegetation are likely to add to urban biodiversity. However, to optimize the microbial benefit of urban greening, it is necessary to understand the factors that regulate microbial diversity, abundance, and community composition within urban green space. Today, as described above, it is known that monocultures, no matter how beautiful, may not be optimal. Urban design should also allow and encourage active physical contacts with green elements (Fig. 3).

3.3   Indoor Interventions

In preindustrial and traditional agricultural societies, human settlements contained vast microbial diversity also indoors (Fig. 2). Today, due to vacuum cleaners and disinfectants, indoor microbial abundance and the proportion of microbiota originating in soil and vegetation are low. Since urbanites spend most of their time indoors, it is unsure whether outdoor interventions can reach the entire urban population. Therefore, it has been hypothesized that the insertion of rich environmental microbiota indoors can enhance immune regulation and decrease the incidence of immune-mediated diseases. So far, only a single study has been reported. Nurminen et al. [85] manufactured a microbiologically rich powder from soil and plant-based organic materials. They instructed volunteers to touch the biodiverse organic soil-like material three times a day (before breakfast, dinner, and going to sleep) for 20 s for 2 weeks. After the exposure period, Nurminen et al. [85] observed increased stool bacterial diversity and a positive association between the increasing diversity of commensal microbiota and immune regulation. Similar studies and at least one large intervention trial in which infants are exposed to rich environmental microbiota for the first year of their life are going on, but so far the results have not been reported in the scientific literature [100]. As the use of biodiversity elements may require a change in living habits, willingness to test and use health-enhancing innovations has been recently explored [101, 102]. The results indicate the crucial role of scientific evidence and give advice on how to design potential future intervention trials [102, 103].

4 Future Perspectives

Nature and greenness are associated with mental well-being, low incidence of immune-mediated diseases, and several other health benefits [23, 97, 104] (other chapters in this book). Despite this, a short distance to coniferous forests predisposed urban dwellers to asthma and allergic rhinitis in a large study that combined several cohorts from various Central and Northern European countries [105]. A potential reason lies in human behavior, i.e., the benefits of nature are received by the minority that visits frequently urban seminatural ecosystems, particularly forests, while those who always prefer urban built areas receive mainly allergens, such as pollen [106]. The current chapter has reviewed research showing the multiple ways how natural microbial communities are distorted in the urban living environment. While it is hard to separate the importance of any single factor, the combined effect of human activities has led to distortion and eradication of original microbial communities in urban neighborhoods.

The crucial question is how to integrate attractive biodiversity hotspots to urban milieu and how to plan vegetation and decomposer networks that flourish under intense use. Weeds are enemies in agricultural fields, but in urban green space, weeds forming runners and root weeds and woody plants resprouting quickly, e.g., willows, dandelions, goatweeds, and their nontoxic colleagues, may provide an option to increase biodiversity in places used frequently by children. Dead wood, sticks, and cones contain a rich degrader community [87], are attractive, and have traditionally been available for children to play and exercise with. Fallen leaves and turfgrass thatch contribute to natural seasonal variation in soil surface microbial communities. These and other ordinary possibilities may turn out to be the easiest and economically sound options for urban rewilding. In addition to these, research is needed to find out how important it is to insert planting boxes and potted trees and bushes, i.e., sources of plant debris and dirt, outside green spaces. In other words, there is no knowledge how dense the green urban network should be to beget health benefits.

An interesting future research direction is the role of *Proteobacteria*, particularly *Gammaproteobacteria* and *Acinetobacter* spp., in immune modulation [107]. Certain *Acinetobacter* strains are known to produce biosurfactants [108]. Biosurfactants allow bacteria to stick tightly on the skin. Studies by Hanski et al. [89], Roslund et al. [78], and several others identify associations between *Proteobacteria*, *Gammaproteobacteria*, or *Acinetobacter* and immune modulation or immune system problems. It is currently not known whether the reason for the associations is related to the ability to stick to the skin, which may have clinical significance, or whether it is a consequence of the dominance of *Proteobacteria* in organic surface soils (see above). Interestingly, proteobacterial microbes did not have associations in the study by Nurminen et al. [85] that used a homogenized mixture of commercially available gardening soils and plant materials, instead of surface soil transferred from the field.

While high hygiene level is mandatory in welfare states, the distortion and destruction of the natural microbial environment, i.e., the ever-changing network of lazy microbial survivors, are not. On the contrary, the need to control biodiversity loss, invasive species, and environmental pollution has been internationally recognized. Sustainable cities and communities are one of the UN sustainability goals, and sustainability in cities is based on welfare of ecosystems. Although the first intervention trials showing the immunomodulatory role of biodiversity have been published [78, 85], there is an urgent need for research on how biodiversity interventions change microbial and vegetation diversity in urban living environments, particularly at playgrounds, daycare units and schools, yards, and parks. The goal of the upcoming research should be to find practical solutions to enrich taxonomic and functional microbiota and to allow the entire urban population to reach the positive health and welfare effects associated with green, biodiverse environments. Notably, as natural ecosystems are diverse, any potential solutions must consider local needs and conditions. Local sources of biodiversity may facilitate successful rewilding of the current low-biodiversity urban settlements.

5   Conclusions

The distortion of the microbiota of the natural environment by humans results from several parallel factors. In addition to direct devastation of greenery and organic ground surface, environmental pollution and exotic, invasive species distort the original microbiota, including the diversity of bacteria associated with health impacts. The distortion of the microbiota of the natural environment is a likely core reason for the high incidence of immune-mediated diseases in urbanized societies. Attempts to rewild urban microbiota and reintroduce natural microbiota to urban areas have shown promising results. The reintroduction must not be limited to existing green areas. Instead, to reach the health benefits, the reintroduction needs to encourage repeated close contacts with dirt, vegetation, and any elements hosting diverse and abundant microbiota. The implementation of this is likely to require large-scale development, production, and dissemination of elements containing diverse microbiota. Optimally, urban dwellers will have plenty of options for safe interaction with diverse environmental microbiota in everyday life.

Compliance with Ethical Standards International and local laws and the ethical standards of the publisher were always followed. When a study by the author's research group recruited human volunteers, the ethical approval was obtained from the ethical committee of the local hospital district (Tampereen yliopistollisen sairaalan erityisvastuualueen alueellinen eettinen toimikunta, Pirkanmaa, Finland). All participants received oral and written information about the study, and they or the parents/guardians of the children provided a written informed consent that was in accordance with the Declaration of Helsinki.

Conflict of Interest Statement The author has been named as an inventor in two patent applications submitted by the University of Helsinki (patent application number 20165932 "Immunomodulatory compositions" and patent application number 20175196 "Immunomodulatory gardening and landscaping material" at the Finnish Patent and Registration Office). The author has not received royalties from the patent applications. The author, jointly with University of Helsinki and other key investigators in the application number 20165932, is a founder and member of the board of Uute Scientific Ltd, which develops biodiversity-based interventions for the prevention of immune-mediated diseases.

References

1. Marchesi JR, Ravel J. The vocabulary of microbiome research: a proposal. Microbiome. 2015;3:31. https://doi.org/10.1186/s40168-015-0094-5.
2. Liang X, Wagner RE, Zhuang J, DeBruyn JM, Wilhelm SW, Liu F, et al. Viral abundance and diversity vary with depth in a southeastern United States agricultural ultisol. Soil Biol Biochem. 2019;137:107546. https://doi.org/10.1016/j.soilbio.2019.107546.
3. Puhakka R, Rantala O, Roslund MI, Rajaniemi J, Laitinen OH, Sinkkonen A, et al. Greening of daycare yards with biodiverse materials affords well-being, play and environmental relationships. Int J Environ Res Public Health. 2019;16(16):2948. https://doi.org/10.3390/ijerph16162948.
4. Tedersoo L, Bahram M, Polme S, Koljalg U, Yorou NS, Wijesundera R, et al. Fungal biogeography. Global diversity and geography of soil fungi. Science. 2014;346(6213):1256688. https://doi.org/10.1126/science.1256688.
5. Tecon R, Or D. Biophysical processes supporting the diversity of microbial life in soil. FEMS Microbiol Rev. 2017;41(5):599–623. https://doi.org/10.1093/femsre/fux039.
6. Thompson LR, Sanders JG, McDonald D, Amir A, Ladau J, Locey KJ, et al. A communal catalogue reveals Earth's multiscale microbial diversity. Nature. 2017;551(7681):457–63. https://doi.org/10.1038/nature24621.
7. Tedersoo L, Bahram M, Zobel M. How mycorrhizal associations drive plant population and community biology. Science. 2020;367(6480):eaba1223. https://doi.org/10.1126/science.aba1223.
8. DeLeo PC, Baveye P, Ghiorse WC. Use of confocal laser scanning microscopy on soil thin-sections for improved characterization of microbial growth in unconsolidated soils and aquifer materials. J Microbiol Methods. 1997;30(3):193–203. https://doi.org/10.1016/S0167-7012(97)00065-1.
9. Hillebrand H. On the generality of the latitudinal diversity gradient. Am Nat. 2004;163(2):192–211. https://doi.org/10.1086/381004.
10. Upton RN, Checinska Sielaff A, Hofmockel KS, Xu X, Polley HW, Wilsey BJ. Soil depth and grassland origin cooperatively shape microbial community co-occurrence and function. Ecosphere. 2020;11(1):e02973. https://doi.org/10.1002/ecs2.2973.
11. Spain AM, Krumholz LR, Elshahed MS. Abundance, composition, diversity and novelty of soil Proteobacteria. ISME J. 2009;3(8):992–1000. https://doi.org/10.1038/ismej.2009.43.

12. Janssen PH. Identifying the dominant soil bacterial taxa in libraries of 16S rRNA and 16S rRNA genes. Appl Environ Microbiol. 2006;72(3):1719–28. https://doi.org/10.1128/AEM.72.3.1719-1728.2006.

13. Laforest-Lapointe I, Paquette A, Messier C, Kembel SW. Leaf bacterial diversity mediates plant diversity and ecosystem function relationships. Nature. 2017;546(7656):145–7. https://doi.org/10.1038/nature22399.

14. Cordier T, Robin C, Capdevielle X, Desprez-Loustau M-L, Vacher C. Spatial variability of phyllosphere fungal assemblages: genetic distance predominates over geographic distance in a European beech stand (Fagus sylvatica). Fungal Ecol. 2012;5(5):509–20. https://doi.org/10.1016/j.funeco.2011.12.004.

15. Darlison J, Mogren L, Rosberg AK, Gruden M, Minet A, Line C, et al. Leaf mineral content govern microbial community structure in the phyllosphere of spinach (Spinacia oleracea) and rocket (Diplotaxis tenuifolia). Sci Total Environ. 2019;675:501–12. https://doi.org/10.1016/j.scitotenv.2019.04.254.

16. Siebert J, Sunnemann M, Auge H, Berger S, Cesarz S, Ciobanu M, et al. The effects of drought and nutrient addition on soil organisms vary across taxonomic groups, but are constant across seasons. Sci Rep. 2019;9(1):639. https://doi.org/10.1038/s41598-018-36777-3.

17. Manzoni S, Katul G. Invariant soil water potential at zero microbial respiration explained by hydrological discontinuity in dry soils. Geophys Res Lett. 2014;41(20):7151–8. https://doi.org/10.1002/2014GL061467.

18. Taketani RG, Lanconi MD, Kavamura VN, Durrer A, Andreote FD, Melo IS. Dry season constrains bacterial phylogenetic diversity in a semi-arid rhizosphere system. Microb Ecol. 2017;73(1):153–61. https://doi.org/10.1007/s00248-016-0835-4.

19. Hamilton WD, Brown SP. Autumn tree colours as a handicap signal. Proc R Soc Lond Ser B Biol Sci. 2001;268(1475):1489–93. https://doi.org/10.1098/rspb.2001.1672.

20. Sinkkonen A. Sexual reproduction advances autumn leaf colours in mountain birch (Betula pubescens ssp. czerepanovii). J Evol Biol. 2006;19(5):1722–4. https://doi.org/10.1111/j.1420-9101.2005.00991.x.

21. Lev-Yadun S, Yamazaki K, Holopainen JK, Sinkkonen A. Spring versus autumn leaf colours: evidence for different selective agents and evolution in various species and floras. Flora: Morphol Distrib Funct Ecol Plants. 2012;207(1):80–5. https://doi.org/10.1016/j.flora.2011.10.007.

22. Mikola J, Silfver T, Paaso U, Possen BJMH, Rousi M. Leaf N resorption efficiency and litter N mineralization rate have a genotypic tradeoff in a silver birch population. Ecology. 2018;99(5):1227–35. https://doi.org/10.1002/ecy.2176.

23. Nurminen N, Cerrone D, Lehtonen J, Parajuli A, Roslund M, Lonnrot M, et al. Land cover of early life environment modulates the risk of type 1 diabetes. Diabetes Care. 2021;44:1506. https://doi.org/10.2337/dc20-1719.

24. Kaiser C, Franklin O, Richter A, Dieckmann U. Social dynamics within decomposer communities lead to nitrogen retention and organic matter build-up in soils. Nat Commun. 2015;6(1):8960. https://doi.org/10.1038/ncomms9960.

25. Coyte KZ, Tabuteau H, Gaffney EA, Foster KR, Durham WM. Microbial competition in porous environments can select against rapid biofilm growth. Proc Natl Acad Sci. 2017;114(2):E161–E70. https://doi.org/10.1073/pnas.1525228113.

26. Lehmann J, Hansel CM, Kaiser C, Kleber M, Maher K, Manzoni S, et al. Persistence of soil organic carbon caused by functional complexity. Nat Geosci. 2020;13(8):529–34. https://doi.org/10.1038/s41561-020-0612-3.

27. Byrd AL, Segre JA. Infectious disease. Adapting Koch's postulates. Science. 2016;351(6270):224–6. https://doi.org/10.1126/science.aad6753.

28. Haahtela T, Alenius H, Lehtimaki J, Sinkkonen A, Fyhrquist N, Hyoty H, et al. Immunological resilience and biodiversity for prevention of allergic diseases and asthma. Allergy. 2021;76:3613. https://doi.org/10.1111/all.14895.

29. Tedersoo L, Bahram M, Cajthaml T, Polme S, Hiiesalu I, Anslan S, et al. Tree diversity and species identity effects on soil fungi, protists and animals are context dependent. ISME J. 2016;10(2):346–62. https://doi.org/10.1038/ismej.2015.116.

30. Lucas J, Bill B, Stevenson B, Kaspari M. The microbiome of the ant-built home: the microbial communities of a tropical arboreal ant and its nest. Ecosphere. 2017;8(2):e01639. https://doi.org/10.1002/ecs2.1639.

31. Berman TS, Laviad-Shitrit S, Lalzar M, Halpern M, Inbar M. Cascading effects on bacterial communities: cattle grazing causes a shift in the microbiome of a herbivorous caterpillar. ISME J. 2018;12(8):1952–63. https://doi.org/10.1038/s41396-018-0102-4.

32. Guimaraes HIP, Santana RH, Silveira R, Pinto OHB, Quirino BF, Barreto CC, et al. Seasonal variations in soil microbiota profile of termite (Syntermes wheeleri) mounds in the Brazilian Tropical savanna. Microorganisms. 2020;8(10):1482. https://doi.org/10.3390/microorganisms8101482.

33. Darwin C. On the origin of species by means of natural selection (1967 facsimile reproduction of 1st edn.). New York, NY: Atheneum; 1859.

34. Fridley JD, Sax DF. The imbalance of nature: revisiting a Darwinian framework for invasion biology. Glob Ecol Biogeogr. 2014;23(11):1157–66. https://doi.org/10.1111/geb.12221.

35. Early R, Bradley BA, Dukes JS, Lawler JJ, Olden JD, Blumenthal DM, et al. Global threats from invasive alien species in the twenty-first century and national response capacities. Nat Commun. 2016;7:12485. https://doi.org/10.1038/ncomms12485.

36. Laongpol C, Suzuki K, Sridith K. Floristic composition of the terrestrial coastal vegetation in Narathiwat, Peninsular Thailand. Thai For Bull (Bot). 2005;0(33):44–70.

37. Laongpol C, Suzuki K, Katzensteiner K, Sridith K. Plant community structure of the coastal vegetation of peninsular Thailand. Thai For Bull (Bot). 2009;(37):106.

38. Maneenoon K, Sirirugsa P, Sridith K. Ethnobotany of Dioscorea L. (Dioscoreaceae), a major food plant of the Sakai tribe at Banthad Range, Peninsular Thailand. Ethnobot Res Appl. 2008;6:385. https://doi.org/10.17348/era.6.0.385-394.

39. Catford JA, Jansson R, Nilsson C. Reducing redundancy in invasion ecology by integrating hypotheses into a single theoretical framework. Divers Distrib. 2009;15(1):22–40. https://doi.org/10.1111/j.1472-4642.2008.00521.x.

40. Darji TB, Adhikari B, Pathak S, Neupane S, Thapa LB, Bhatt TD, et al. Phytotoxic effects of invasive Ageratina adenophora on two native subtropical shrubs in Nepal. Sci Rep. 2021;11(1):13663. https://doi.org/10.1038/s41598-021-92791-y.

41. Godoy O, Castro-Diez P, Van Logtestijn RS, Cornelissen JH, Valladares F. Leaf litter traits of invasive species slow down decomposition compared to Spanish natives: a broad phylogenetic comparison. Oecologia. 2010;162(3):781–90. https://doi.org/10.1007/s00442-009-1512-9.

42. Thapa LB, Kaewchumnong K, Sinkkonen A, Sridith K. Plant invasiveness and target plant density: high densities of native Schima wallichii seedlings reduce negative effects of invasive Ageratina adenophora. Weed Res. 2017;57(2):72–80. https://doi.org/10.1111/wre.12238.

43. Thapa L, Kaewchumnong K, Sinkkonen A, Sridith K. Plant communities and Ageratina adenophora invasion in lower montane vegetation, central Nepal. Int J Ecol Dev. 2016;31:35–49.

44. Thapa LB, Kaewchumnong K, Sinkkonen A, Sridith K. "Soaked in rainwater" effect of Ageratina adenophora on seedling growth and development of native tree species in Nepal. Flora. 2020;263:151554. https://doi.org/10.1016/j.flora.2020.151554.

45. Weir BS, Turner SJ, Silvester WB, Park DC, Young JM. Unexpectedly diverse Mesorhizobium strains and Rhizobium leguminosarum nodulate native legume genera of New Zealand, while introduced legume weeds are nodulated by Bradyrhizobium species. Appl Environ Microbiol. 2004;70(10):5980–7. https://doi.org/10.1128/aem.70.10.5980-5987.2004.

46. Sinkkonen A, Laitinen OH, Leppiniemi J, Vauramo S, Hytönen VP, Setälä H. Positive association between biotin and the abundance of root-feeding nematodes. Soil Biol Biochem. 2014;73:93–5. https://doi.org/10.1016/j.soilbio.2014.02.002.

47. Laitinen OH, Kuusela TP, Kukkurainen S, Nurminen A, Sinkkonen A, Hytonen VP. Bacterial avidins are a widely distributed protein family in Actinobacteria, Proteobacteria and Bacteroidetes. BMC Ecol Evol. 2021;21(1):53. https://doi.org/10.1186/s12862-021-01784-y.

48. NOBANIS. Invasive alien species fact sheet – Lupinus polyphyllus. Online Database of the European Network on Invasive Alien Species – NOBANIS. 2010. www.nobanis.org. https://www.nobanis.org/globalassets/speciesinfo/l/lupinus-polyphyllus/lupinus-polyphyllus.pdf. Accessed 18 Jul 2021.

49. Vetter VMS, Tjaden NB, Jaeschke A, Buhk C, Wahl V, Wasowicz P, et al. Invasion of a legume ecosystem engineer in a cold biome alters plant biodiversity. Front Plant Sci. 2018;9:715. https://doi.org/10.3389/fpls.2018.00715.

50. Oosterbeek M, Lozano-Torres JL, Bakker J, Goverse A. Sedentary plant-parasitic nematodes alter auxin homeostasis via multiple strategies. Front Plant Sci. 2021;12:668548. https://doi.org/10.3389/fpls.2021.668548.

51. Ehrenfeld J. Effect of exotic plant invasion on soil nutrient cycling processes. Ecosystems. 2003;6:503–23. https://doi.org/10.1007/s10021-002-0151-3.

52. Lange M, Eisenhauer N, Sierra CA, Bessler H, Engels C, Griffiths RI, et al. Plant diversity increases soil microbial activity and soil carbon storage. Nat Commun. 2015;6:6707. https://doi.org/10.1038/ncomms7707.

53. Laaksonen P, Sinkkonen A, Zaitsev G, Mäkinen E, Grönroos T, Romantschuk M. Treatment of municipal wastewater in full-scale on-site sand filter reduces BOD efficiently but does not reach requirements for nitrogen and phosphorus removal. Environ Sci Pollut Res. 2017;24(12):11446–58. https://doi.org/10.1007/s11356-017-8779-x.

54. Plociniczak T, Sinkkonen A, Romantschuk M, Sulowicz S, Piotrowska-Seget Z. Rhizospheric bacterial strain Brevibacterium casei MH8a colonizes plant tissues and enhances Cd, Zn, Cu phytoextraction by white mustard. Front Plant Sci. 2016;7:101. https://doi.org/10.3389/fpls.2016.00101.

55. Wang Y, Li P, Jiang Z, Sinkkonen A, Wang S, Tu J, et al. Microbial community of high arsenic groundwater in agricultural irrigation area of hetao plain, Inner Mongolia. Front Microbiol. 2016;7:1917. https://doi.org/10.3389/fmicb.2016.01917.

56. Sinkkonen A, Kauppi S, Pukkila V, Nan H, Płociniczak T, Kontro M, et al. Previous exposure advances the degradation of an anthropogenic s-triazine regardless of soil origin. J Soils Sediments. 2013;13(8):1430–8. https://doi.org/10.1007/s11368-013-0742-y.

57. Sinkkonen A, Ollila S, Romantschuk M. Changes in TcpA gene frequency explain 2,4,6-trichlorophenol degradation in mesocosms. J Environ Sci Health B. 2014;49(10):756–9. https://doi.org/10.1080/03601234.2014.929865.

58. Sun Y, Romantschuk M, Bang-Andreasen T, Rantalainen A-L, Sinkkonen A. Nitrogen fertilizers stimulate desorption and biodegradation of gasoline aromatics in the soil from high Arctic permafrost active layer: a laboratory study. Int Biodeterior Biodegradation. 2020;150:104957. https://doi.org/10.1016/j.ibiod.2020.104957.

59. Liu X, Selonen V, Steffen K, Surakka M, Rantalainen A-L, Romantschuk M, et al. Meat and bone meal as a novel biostimulation agent in hydrocarbon contaminated soils. Chemosphere. 2019;225:574–8. https://doi.org/10.1016/j.chemosphere.2019.03.053.

60. Mikkonen A, Ylaranta K, Tiirola M, Dutra LAL, Salmi P, Romantschuk M, et al. Successful aerobic bioremediation of groundwater contaminated with higher chlorinated phenols by indigenous degrader bacteria. Water Res. 2018;138:118–28. https://doi.org/10.1016/j.watres.2018.03.033.

61. Parajuli A, Grönroos M, Kauppi S, Płociniczak T, Roslund MI, Galitskaya P, et al. The abundance of health-associated bacteria is altered in PAH polluted soils-Implications for health in urban areas? PLoS One. 2017;12(11):e0187852. https://doi.org/10.1371/journal.pone.0187852.

62. Roslund MI, Grönroos M, Rantalainen AL, Jumpponen A, Romantschuk M, Parajuli A, et al. Half-lives of PAHs and temporal microbiota changes in commonly used urban landscaping materials. PeerJ. 2018;6:e4508. https://doi.org/10.7717/peerj.4508.

63. Yan Z-Z, Chen Q-L, Zhang Y-J, He J-Z, Hu H-W. Industrial development as a key factor explaining variances in soil and grass phyllosphere microbiomes in urban green spaces. Environ Pollut. 2020;261:114201. https://doi.org/10.1016/j.envpol.2020.114201.

64. Sorbo S, Sinkkonen A, Aprile G, Strumia S, Cobianchi RC, Leone A, et al. Ultrastructural effects of trace elements and environmental pollution in Italian "Triangle of Death" on Pseudevernia furfuracea (L.) Zopf. Plant Biosyst. 2011;145:461–71.

65. Hansi M, Weidenhamer JD, Sinkkonen A. Plant growth responses to inorganic environmental contaminants are density-dependent: experiments with copper sulfate, barley and lettuce. Environ Pollut. 2014;184:443–8. https://doi.org/10.1016/j.envpol.2013.09.027.

66. Belz RG, Patama M, Sinkkonen A. Low doses of six toxicants change plant size distribution in dense populations of Lactuca sativa. Sci Total Environ. 2018;631-632:510–23. https://doi.org/10.1016/j.scitotenv.2018.02.336.

67. Kauppi S, Romantschuk M, Strömmer R, Sinkkonen A. Natural attenuation is enhanced in previously contaminated and coniferous forest soils. Environ Sci Pollut Res. 2012;19(1):53–63. https://doi.org/10.1007/s11356-011-0528-y.

68. Sinkkonen A, Kauppi S, Simpanen S, Rantalainen AL, Strommer R, Romantschuk M. Layer of organic pine forest soil on top of chlorophenol-contaminated mineral soil enhances contaminant degradation. Environ Sci Pollut Res Int. 2013;20(3):1737–45. https://doi.org/10.1007/s11356-012-1047-1.

69. Roslund MI, Rantala S, Oikarinen S, Puhakka R, Hui N, Parajuli A, et al. Endocrine disruption and commensal bacteria alteration associated with gaseous and soil PAH contamination among daycare children. Environ Int. 2019;130:104894. https://doi.org/10.1016/j.envint.2019.06.004.

70. Wang C, Xu CX, Krager SL, Bottum KM, Liao DF, Tischkau SA. Aryl hydrocarbon receptor deficiency enhances insulin sensitivity and reduces PPAR-α pathway activity in mice. Environ Health Perspect. 2011;119(12):1739–44. https://doi.org/10.1289/ehp.1103593.

71. Borland MG, Krishnan P, Lee C, Albrecht PP, Shan W, Bility MT, et al. Modulation of aryl hydrocarbon receptor (AHR)-dependent signaling by peroxisome proliferator-activated receptor β/δ (PPARβ/δ) in keratinocytes. Carcinogenesis. 2014;35(7):1602–12. https://doi.org/10.1093/carcin/bgu067.

72. Zhang Y, Dong S, Wang H, Tao S, Kiyama R. Biological impact of environmental polycyclic aromatic hydrocarbons (ePAHs) as endocrine disruptors. Environ Pollut. 2016;213:809–24. https://doi.org/10.1016/j.envpol.2016.03.050.

73. Vari HK, Roslund MI, Oikarinen S, Nurminen N, Puhakka R, Parajuli A, et al. Associations between land cover categories, gaseous PAH levels in ambient air and endocrine signaling predicted from gut bacterial metagenome of the elderly. Chemosphere. 2021;265:128965. https://doi.org/10.1016/j.chemosphere.2020.128965.

74. Zhao Q, Xiong W, Xing Y, Sun Y, Lin X, Dong Y. Long-term coffee monoculture alters soil chemical properties and microbial communities. Sci Rep. 2018;8(1):6116. https://doi.org/10.1038/s41598-018-24537-2.

75. Kavamura VN, Mendes R, Bargaz A, Mauchline TH. Defining the wheat microbiome: towards microbiome-facilitated crop production. Comput Struct Biotechnol J. 2021;19:1200–13. https://doi.org/10.1016/j.csbj.2021.01.045.

76. Stein MM, Hrusch CL, Gozdz J, Igartua C, Pivniouk V, Murray SE, et al. Innate immunity and asthma risk in amish and hutterite farm children. N Engl J Med. 2016;375(5):411–21. https://doi.org/10.1056/NEJMoa1508749.

77. Parajuli A, Hui N, Puhakka R, Oikarinen S, Grönroos M, Selonen VAO, et al. Yard vegetation is associated with gut microbiota composition. Sci Total Environ. 2020;713:136707. https://doi.org/10.1016/j.scitotenv.2020.136707.

78. Roslund MI, Puhakka R, Grönroos M, Nurminen N, Oikarinen S, Gazali AM, et al. Biodiversity intervention enhances immune regulation and health-associated commensal microbiota among daycare children. Sci Adv. 2020;6(42):eaba2578. https://doi.org/10.1126/sciadv.aba2578.

79. Sharma ML, Herne DE, Byrne JD, Kin PG. Nutrient discharge beneath urban lawns to a sandy coastal Aquifer, Perth, Western Australia. Hydrogeol J. 1996;4(1):103–17. https://doi.org/10.1007/s100400050100.

80. Byrne L, Bruns M, Kim KC. Ecosystem properties of urban land covers at the aboveground–belowground interface. Ecosystems. 2008;11:1065–77. https://doi.org/10.1007/s10021-008-9179-3.

81. Newbound M, McCarthy MA, Lebel T. Fungi and the urban environment: a review. Landsc Urban Plan. 2010;96(3):138–45. https://doi.org/10.1016/j.landurbplan.2010.04.005.

82. Dorado-Morales P, Vilanova C, Pereto J, Codoner FM, Ramon D, Porcar M. A highly diverse, desert-like microbial biocenosis on solar panels in a Mediterranean city. Sci Rep. 2016;6: 29235. https://doi.org/10.1038/srep29235.

83. Hui N, Grönroos M, Roslund MI, Parajuli A, Vari HK, Soininen L, et al. Diverse environmental microbiota as a tool to augment biodiversity in urban landscaping materials. Front Microbiol. 2019;10:536. https://doi.org/10.3389/fmicb.2019.00536.

84. Gronroos M, Parajuli A, Laitinen OH, Roslund MI, Vari HK, Hyoty H, et al. Short-term direct contact with soil and plant materials leads to an immediate increase in diversity of skin microbiota. Microbiologyopen. 2019;8(3):e00645. https://doi.org/10.1002/mbo3.645.

85. Nurminen N, Lin J, Grönroos M, Puhakka R, Kramna L, Vari HK, et al. Nature-derived microbiota exposure as a novel immunomodulatory approach. Future Microbiol. 2018;13: 737–44. https://doi.org/10.2217/fmb-2017-0286.

86. Selway CA, Mills JG, Weinstein P, Skelly C, Yadav S, Lowe A, et al. Transfer of environmental microbes to the skin and respiratory tract of humans after urban green space exposure. Environ Int. 2020;145:106084. https://doi.org/10.1016/j.envint.2020.106084.

87. Korhonen A, Siitonen J, Kotze DJ, Immonen A, Hamberg L. Stand characteristics and dead wood in urban forests: potential biodiversity hotspots in managed boreal landscapes. Landsc Urban Plan. 2020;201:103855. https://doi.org/10.1016/j.landurbplan.2020.103855.

88. Cadenasso M, Pickett STA. Urban principles for ecological landscape design and maintenance: scientific fundamentals. Cities Environ. 2008;1:4. https://doi.org/10.15365/cate.1242008.

89. Hanski I, von Hertzen L, Fyhrquist N, Koskinen K, Torppa K, Laatikainen T, et al. Environmental biodiversity, human microbiota, and allergy are interrelated. Proc Natl Acad Sci U S A. 2012;109(21):8334–9. https://doi.org/10.1073/pnas.1205624109.

90. Parajuli A, Grönroos M, Siter N, Puhakka R, Vari HK, Roslund MI, et al. Urbanization reduces transfer of diverse environmental microbiota indoors. Front Microbiol. 2018;9:84. https://doi.org/10.3389/fmicb.2018.00084.

91. Hui N, Parajuli A, Puhakka R, Gronroos M, Roslund MI, Vari HK, et al. Temporal variation in indoor transfer of dirt-associated environmental bacteria in agricultural and urban areas. Environ Int. 2019;132:105069. https://doi.org/10.1016/j.envint.2019.105069.

92. Leung MH, Wilkins D, Li EK, Kong FK, Lee PK. Indoor-air microbiome in an urban subway network: diversity and dynamics. Appl Environ Microbiol. 2014;80(21):6760–70. https://doi.org/10.1128/AEM.02244-14.

93. Salim SY, Kaplan GG, Madsen KL. Air pollution effects on the gut microbiota: a link between exposure and inflammatory disease. Gut Microbes. 2014;5(2):215–9. https://doi.org/10.4161/gmic.27251.

94. Kirjavainen PV, Karvonen AM, Adams RI, Taubel M, Roponen M, Tuoresmaki P, et al. Farm-like indoor microbiota in non-farm homes protects children from asthma development. Nat Med. 2019;25(7):1089–95. https://doi.org/10.1038/s41591-019-0469-4.

95. UNEP-WCMC. United Nations list of protected areas. Supplement on protected area management effectiveness. Cambridge: UNEP-WCMC; 2018. p. 2018.

96. Watkins H, Robinson JM, Breed MF, Parker B, Weinstein P. Microbiome-inspired green infrastructure: a toolkit for multidisciplinary landscape design. Trends Biotechnol. 2020;38 (12):1305–8. https://doi.org/10.1016/j.tibtech.2020.04.009.

97. Ojala A, Korpela K, Tyrvainen L, Tiittanen P, Lanki T. Restorative effects of urban green environments and the role of urban-nature orientedness and noise sensitivity: a field experiment. Health Place. 2019;55:59–70. https://doi.org/10.1016/j.healthplace.2018.11.004.

98. Lehtimäki J, Sinkko H, Hielm-Björkman A, Laatikainen T, Ruokolainen L, Lohi H. Simultaneous allergic traits in dogs and their owners are associated with living environment, lifestyle and microbial exposures. Sci Rep. 2020;10(1):21954. https://doi.org/10.1038/s41598-020-79055-x.

99. Saarenpää M, Roslund MI, Puhakka R, Grönroos M, Parajuli A, Hui N, et al. Do rural second homes shape commensal microbiota of urban dwellers? A pilot study among urban elderly in Finland. Int J Environ Res Public Health. 2021;18(7):3742.

100. Prescott SL, Hancock T, Bland J, van den Bosch M, Jansson JK, Johnson CC, et al. Eighth Annual Conference of inVIVO Planetary Health: from challenges to opportunities. Int J Environ Res Public Health. 2019;16(21):4302.

101. Puhakka R, Valve R, Sinkkonen A. Older consumers' perceptions of functional foods and non-edible health-enhancing innovations. Int J Consum Stud. 2018;42(1):111–9. https://doi.org/10.1111/ijcs.12400.

102. Puhakka R, Haskins AH, Jauho M, Grönroos M, Sinkkonen A. Factors affecting young adults' willingness to try novel health-enhancing nature-based products. J Int Consum Mark. 2021;33:595. https://doi.org/10.1080/08961530.2021.1873887.

103. Puhakka R, Ollila S, Valve R, Sinkkonen A. Consumer trust in a health-enhancing innovation – comparisons between Finland, Germany, and the United Kingdom. J Int Consum Mark. 2019;31(2):162–76. https://doi.org/10.1080/08961530.2018.1498757.

104. Dzhambov AM, Browning M, Markevych I, Hartig T, Lercher P. Analytical approaches to testing pathways linking greenspace to health: a scoping review of the empirical literature. Environ Res. 2020;186:109613. https://doi.org/10.1016/j.envres.2020.109613.

105. Parmes E, Pesce G, Sabel CE, Baldacci S, Bono R, Brescianini S, et al. Influence of residential land cover on childhood allergic and respiratory symptoms and diseases: evidence from 9 European cohorts. Environ Res. 2020;183:108953. https://doi.org/10.1016/j.envres.2019.108953.

106. Kasprzyk I, Ćwik A, Kluska K, Wójcik T, Cariñanos P. Allergenic pollen concentrations in the air of urban parks in relation to their vegetation. Urban For Urban Green. 2019;46:126486. https://doi.org/10.1016/j.ufug.2019.126486.

107. Prescott SL, Larcombe DL, Logan AC, West C, Burks W, Caraballo L, et al. The skin microbiome: impact of modern environments on skin ecology, barrier integrity, and systemic immune programming. World Allergy Organ J. 2017;10(1):29. https://doi.org/10.1186/s40413-017-0160-5.

108. Zhao Z, Wong JW. Biosurfactants from Acinetobacter calcoaceticus BU03 enhance the solubility and biodegradation of phenanthrene. Environ Technol. 2009;30(3):291–9. https://doi.org/10.1080/09593330802630801.