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Our interface with the built environment: immunity and the indoor microbiota

Simon Lax[1,2], **Cathryn R. Nagler**[3], and **Jack A. Gilbert**[1,2,4,5]

[1]Institute for Genomic and Systems Biology, Biosciences Department, Argonne National Laboratory, 9700 South Cass Avenue, Argonne, IL 60439, USA

[2]Department of Ecology and Evolution, University of Chicago, 1101 East 57th Street, Chicago, IL 60637, USA

[3]Committee on Immunology, Department of Pathology, University of Chicago, 924 East 57th Street, Chicago, IL 60637, USA

[4]Marine Biological Laboratory, 7 MBL Street, Woods Hole, MA 02543, USA

[5]College of Environmental and Resource Sciences, Zhejiang University, Hangzhou, 310058, China

Abstract

The rise of urbanization and an increasingly indoor life-style has affected human interactions with our microbiota in unprecedented ways. We discuss how this lifestyle may influence immune development and function, and argue that it is time that we examined ways to manipulate the indoor environment to increase our exposure to a wider phylogeny of microorganisms. An important step is to continue to engage citizen scientists in the efforts to characterize our interactions with the diverse microbial environments that we inhabit.

Keywords

microbiome; built environment

Over the past 150 years we have become an indoor species. For many of us, our natural ecosystem has been restricted to the built environment, especially in the developed world, where an average of 90% of our lives takes place indoors. Modern buildings are equipped with surfaces and environmental systems designed to reduce the potential for microbial life to flourish. This fundamental shift in our lifestyle is likely impacting on the development and function of our immune systems in ways that we are only beginning to understand.

Humans are born mostly microbially sterile [1], and the subsequent microbial colonization and succession within and on our bodies is influenced by our interaction with the world into which we are thrust. This interaction can take many shapes, including physical interaction with other humans, ingesting breast milk which contains a complex microbiota [2], putting

Corresponding author: Gilbert, J.A. (gilbertjack@anl.gov)..

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foreign objects in our mouths, interacting with the outdoor environment, and consuming food and water. All these interactions can act as sources that shape our microbial selves, such that the extraordinary number of permutations of potential microbial interactions with our environments leads to the development of a unique microbiota in every person. Even identical twins do not share any greater microbial similarity than normal siblings [3], which suggests a degree of stochasticity of taxonomic succession that is independent of host genetics. However, this could be misinterpreted as suggesting that the host (human) system does not select for favorable microbial features from the constant bombardment it encounters. Nothing could be further from the truth. The human immune system exhibits a complex and dynamic relationship with the microbiota, that results in microbial taxa with favorable qualities being recruited. The ability of intestinal regulatory T cells to promote bacterial diversity by controlling the production of IgA is an ideal example of this process [4] (Box 1).

Because the diversity of environmental sources we interact with may influence the colonization and succession of our microbiota from birth to a stable adult state [5], it is likely that if the diversity of sources we are exposed to were to decline, so too would the repertoire of our microbial taxonomy. Reducing the humidity in the air through air conditioning, and reducing the availability of complex substrates (e.g., soil) or porous surfaces (e.g., wood) through choices in building materials, are likely to significantly impact not only on microbial biomass but also on the diversity of the microbiota that can actively grow. This in turn is likely to significantly influence the source of our bodily microbiome, which could have untold consequences for our physiological, immunological, and neurological development.

When a person grows up within an urban environment they are exposed to a myriad of potential insults to their health, but the impact of being exposed to a reduced diversity of microorganisms (let alone from an assemblage of taxa that is likely experiencing an extraordinary disrupted ecology) has not been properly explored. The microbial ecology of the built and urban environment is a brave new frontier of microbiology. We understand very little about how these communities assemble and evolve, how they differ from natural environments with regard to their ecological stability and functional potential, and what role they may play in human social ecology. The urban ecosystem is growing more rapidly than virtually any other environment on Earth, and consequently is home to an ever-increasing proportion of humanity. As this new environment emerges microbes will colonize and adapt to the myriad niches provided, and are therefore likely to develop novel ecologies, and potentially evolutionary trajectories, that could interact with humanity in many ways. It is clear that choices in architectural design and building materials can significantly affect the microbial communities we interact with on a daily basis [6,7]. Harnessing the true potential of cities to provide services for their developing population density will require a fundamental understanding not only of the social and economic interactions we have with this environment but also of biological relationships, especially regarding our ability to harvest food from urban centers.

Recent studies have focused on characterizing the basic ecological structure of the indoor and urban environment [8]. From investigations of airplanes, kitchens, offices, restrooms,

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and hospital wards, it is apparent that the human microbiome comprises the major microbial source for these indoor systems [7,9]. This is unsurprising because we are hypothesized to shed millions of microbial cells hourly into our local environment. The built environment usually has limited circulation and exchange with the outdoors, and such dispersal is highly likely to build up in our built spaces. Indeed, recent work on the microbiology of our homes over time suggests that we colonize the microbial niches of an indoor space with our own microbiota within 24 h [9]. Interestingly, in this same study, the microbial signature within each household was directly attributable to the microbial signature of its occupants. This suggests that, within a given property, the major microbial source you will be exposed to is your own. Such a self-perpetuating system is likely to have consequences, which could be negative if your microbiota is in dysbiosis with your own body. If an infant is growing up in such a space, its immune system will be trained by, and adapt to, this simplified and self-reinforcing microbial ecosystem. It is possible that this may result in a perpetuation of environmentally driven immunological and neurological conditions within families, such as asthma, allergies, and even depression. Recent work has demonstrated that the reintroduction of key bacteria can help to alleviate the symptoms of asthma and allergies in animal models [10,11], which suggests hope for the development of clinical probiotics to alleviate these conditions. However, based on the interface we have with the built environment, it is also time we examined ways to manipulate this environment to create a greater diversity of sources that can help to increase our exposure to a wider phylogeny of microorganisms from birth and, in this way, contribute to health. The Hospital Microbiome Project (http://www.hospitalmicrobiome.com) was designed to determine how the microbial community of a hospital develops, and how interacts with the human population. By better understanding the successional ecology and the existence of stable ecological states in the hospital microbiome, we will be better placed to develop architectural and engineering solutions to create an environmental microbial ecology that may help to support healthy immune system interaction. This is especially important for hospitals because patients are often under extreme physical stress, as is their microbiota. Treatment with antibiotics and physical surgery can lead to the development of a pathobiome with negative health implications for the patient [12]. If the patients were provided a course of designed probiotics and an environment that promoted the colonization of their bodies with an appropriate microbiota, it is possible that patients might experience enhanced recovery.

If we are to characterize the ecology of the unique microbial world we all live in, it is essential that we work with as diverse a range of individuals as possible, and harness the efforts of the growing community of citizen scientists (Box 2). Observational studies from people and their built environments have played a major role in advancing our understanding of the breadth of microbial diversity across these environments. Citizen scientists have been instrumental in gathering evidence about the human and built environment, providing an exciting opportunity for scientific exploration and educational out-reach. Working with the public to implement experimental designs that can address questions we have about built-environment ecology has been highly successful, enabling us to broaden the research framework in which we test hypotheses. Although such investigation modalities are difficult to control, and can result in a higher degree of variance being attributable to sampling error or sample-storage differences than would be expected during

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laboratory-based studies, the value of distributed data collection, and the potential to integrate research into the community, far outweigh these problems, which can mostly be solved through appropriate statistical design.

The urban and built microbiome undoubtedly plays a role in the development of our microbiota, and is therefore likely to influence the development or response of our immune systems. Our capacity to alleviate immunological pathologies will be predicated on our understanding of the microbial drivers of these conditions, and of how we can redress the microbial equilibrium of our built environment.

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Box 1. How does the body recruit a microbiome?

We acquire our founding microbiota during passage through the vaginal canal; babies born via Caesarean section have an initial microbiota dominated, instead, by bacteria typically associated with the skin [13]. The comparatively limited neonatal microbiota increases in diversity as environmental exposure accumulates with age. Infancy and early childhood is a time of great plasticity for the developing microbiota, which is readily altered by environmental stimuli including infection, changes in diet, or treatment with antibiotics. Disruption of the neonatal microbiota can have long-lasting consequences for the homeostatic host-microbe relationship. For example, recent work shows that neonatal antibiotic treatment induces changes in the microbial metabolome, and this promotes obesity [14] and depletes mucosa-associated bacteria crucial for fortifying the epithelial barrier to prevent allergic sensitization to food [11]. The microbiota of an individual stabilizes with adulthood but continues to be shaped by environmental stimuli. The intestinal microbiota characteristic of modern urban settings differs dramatically from that found in individuals living in rural pre-industrialized societies [15], and is associated with the increasing prevalence of diseases common to the 21st century lifestyle including diabetes, inflammatory bowel disease, obesity, allergies, and asthma.

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Box 2. How are citizen scientists contributing to discovery?

Recent studies of the built environment, such as the home microbiome project (http://www.homemicrobiome.com) [9] have acquired samples from individuals, couples, and families across the USA by reaching out to the through Facebook (https://www.facebook.com/HomeMicrobiome) and Twitter (@homemicrobiome). Interested volunteers were vetted and, if they were considered appropriate, were trained and sent a small freezer and a package of sampling kits with instructions on how to sample themselves, and what information to record (Figure I). This outreach enabled the study to acquire a geographically and culturally diverse group of participants, which increased the power of the study. Importantly, through studies such as American Gut (http://www.americangut.org), we are enabling citizen scientists to both fund the research and be part of the study. Individuals pay $99 to have their microbiome sequenced, and in doing so help to fund the development of a core database of human microbiome samples from thousands of individuals, families, and groups across the USA. Each participant is given basic information on their microbial consortia, and how this compares to the rest of the study. These public outreach efforts help the population to significantly contribute to scientific investigation, mutually benefiting participants and microbial science.

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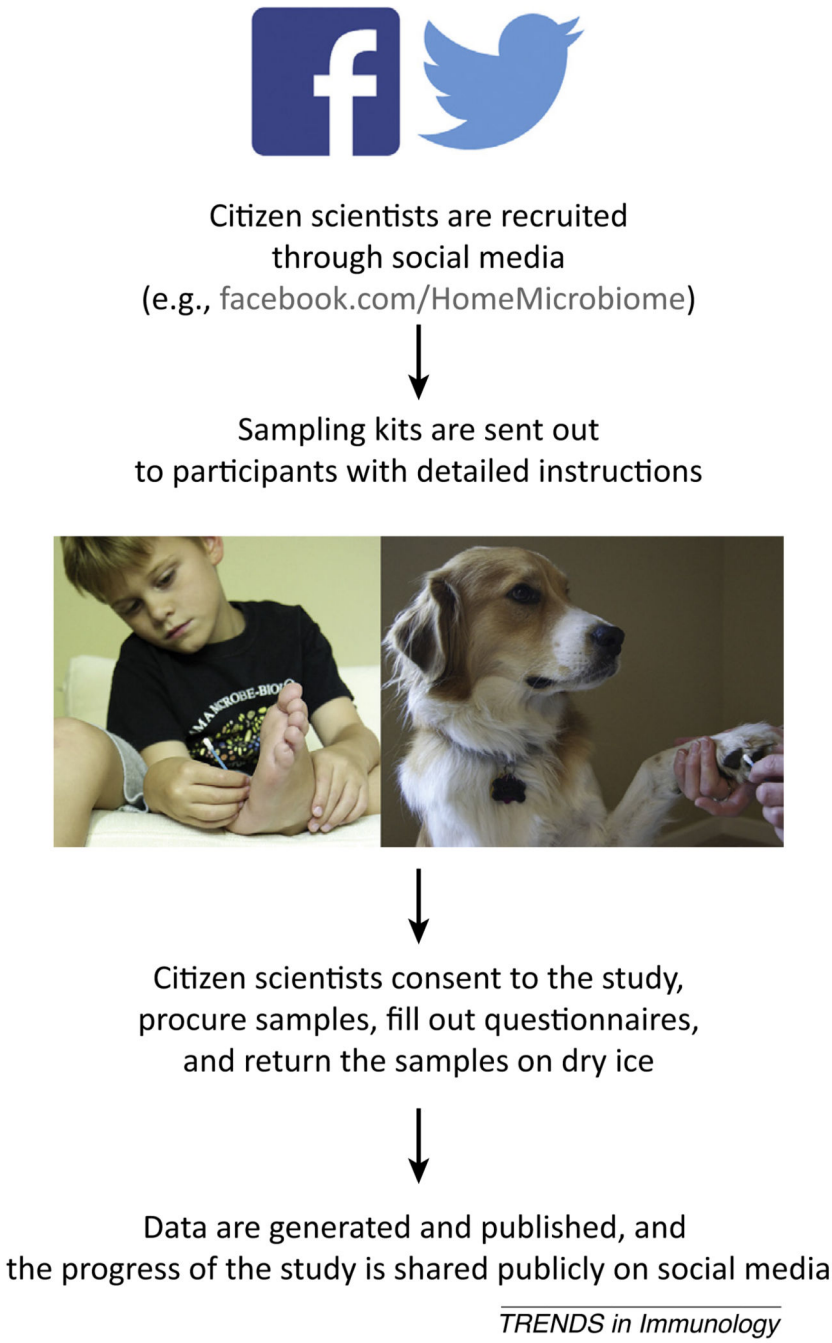

Figure I.

Citizen scientists for the Home Microbiome Project (http://www.homemicrobiome.com) were reached by advertising on social media platforms (e.g., @homemicrobiome and https://www.facebook.com/HomeMicrobiome) and programs such as SciStarter (http://scistarter.com/project/562-Home%20Microbiome%20Study). Interested parties contacted us by email or through the media and were interviewed on the phone or via email to determine their reasons and suitability for inclusion. Accepted participants were consented through an institutional review board (IRB) and then sent sampling kits (containing a description of

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what they should do and sterile synthetic material swabs moistened with saline solution), a small freezer for onsite storage, and a brief questionnaire. Samples were returned to our laboratory at Argonne National Labs (http://www.anl.gov) and processed by extracting the DNA and amplifying the 16S rRNA gene by PCR. These amplicons and the raw DNA were then sequenced to produce 16S rRNA and shotgun metagenomic sequence data. These data were analyzed and used for publication, while simultaneously being communicated directly to the participants. Participants were also contacted following publication to allow them to fully understand how their data were used, and what the final published results showed in terms of advancing science. While the raw sequence data were published on data archive sites (e.g., The NCBI Short Read Archive; http://www.ncbi.nlm.nih.gov/sra) the results were published through the scientific literature, traditional media (e.g., http://phenomena.nationalgeographic.com/2014/08/28/we-constantly-imprint-our-homes-with-our-microbes/), and Facebook (e.g., https://www.facebook.com/HomeMicrobiome). Photos courtesy of Katharine Gilbert.