

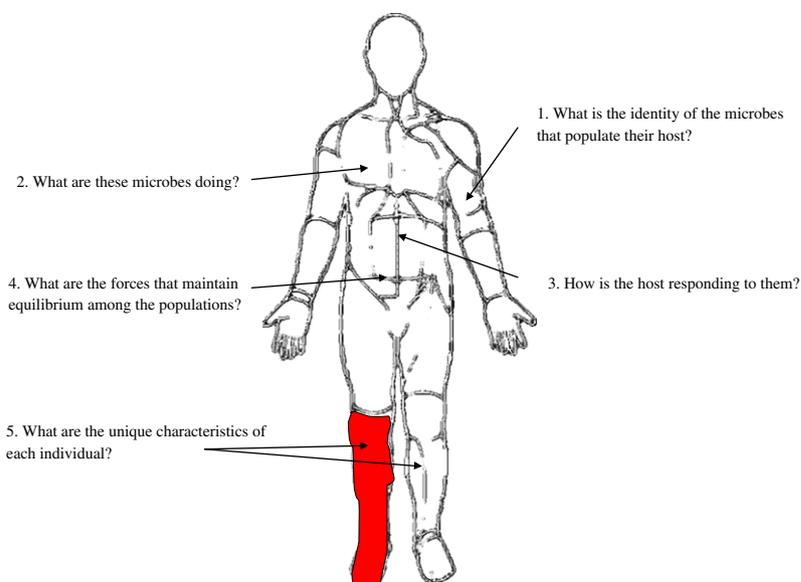
# Harnessing the power of the human microbiome

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Since the earliest days of microbiology, it has been clear that all humans carry many of the same microbial lineages. We now call the collection of microbes living in or on our bodies the human microbiome (1), and a large international effort, called the Human Microbiome Project (HMP) by the National Institutes of Health (2), and known more broadly as the International Human Microbiome Consortium (IHMC), is aimed at its characterization. Studies over the past 5 years focusing on the bacteria present in human skin, for example, indicate that in addition to conserved organisms, there is enormous diversity in identities and abundances (3–6). In part, our appreciation of the conservation and diversity is a function of the level at which the microbiome is being observed. At the phylum level, humans are remarkably similar to one another [and to other mammals (7)], whereas at the genus, species, and strain population levels, the diversity is highly specific for each individual (3–6). A very recent study shows that even for 57 gut bacterial species present in >90% of 124 sampled persons, their estimated abundances varied by 12- to 2,000-fold (8). The challenge is: How can we make sense of our microbial and metagenomic diversity and, importantly, use the information to improve the human condition? In this issue of PNAS, Fierer et al. (9) advance our knowledge of skin-associated bacterial communities and provide a forensic approach that opens new doors of inquiry.

Animals and their resident microbes have coexisted for at least a billion years (10). To understand their relationships, we can ask a series of fundamental biological questions (Fig. 1). Currently, there is extensive interest in obtaining a census of bacteria populating the different niches in various individuals (question 1). This area is advancing well, at least in part because the analytical and computational tools are well formed to answer such questions (8, 11). More important is to understand the physiochemical and metabolic activities (8, 12) of the microbiota (question 2) because these are more biologically significant than census taking. For example, the skin has many important functions critical to host survival, including protection against pathogens and physical agents, metabolic synthesis and storage, heat regulation, and sensation. What roles do our cutaneous microbiota have in these



**Fig. 1.** Five fundamental biological questions that underlie the Human Microbiome Project. Initially, answers are phenomenologic but ultimately must be understood in the context of evolutionary processes. Along the way, myriad applications will be discovered. The red leg represents about 1/10 of the human body, symbolizing  $10^{13}$  human cells in a host with  $10^{14}$  microbial cells (10).

processes, up until now considered exclusively in the host domain?

Host responses (question 3) may be immunologic, metabolic, and/or physical (e.g., peristaltic motion, sloughing of cells), and ultimately are important in understanding both health and disease. The conservation of microbes across most hosts, and over long time periods, implies a biological equilibrium (question 4), but there has been little analysis of the forces that create and maintain specific equilibria (13). As more information is revealed, the framework for the relationship may become more apparent. In total, each individual is the summation of all of the ground rules, circumstances, activities, and interactions (question 5); the characteristics of our genome and microbiome and their interactions in large measure define our individual uniqueness (14–16).

After the 2001 anthrax bioterrorism attacks, scientists saw the need for having reliable and validated procedures for tracking microbial “suspects” and identifying their “hideout,” but also considered that the need for such procedures is much more general (17, 18). How can one “fingerprint” a microbe (17)? Microbial forensics had its origins in molecular epidemiology, using molecular (often DNA based) techniques to solve questions of

disease extent and the spread and transmission of individual microbial species.

In this issue of PNAS, Fierer et al. (9) explore whether the microbial characteristics of the residue of human fingers and hands left on inanimate objects leave a sufficient pattern that can be used to create a microbial fingerprint useful for forensic purposes. This is a novel application, and is particularly remarkable because most prior studies that examined the conjunction of bacteria and fingertips sought ways to remove bacteria, or to prevent their transmission, especially nosocomial pathogens, from fingers to mouth, for example (19, 20). Although preliminary, the work of Fierer et al. (9) is soundly based on techniques and analyses that the group has pioneered (4, 6, 7, 11), and points the way in which microbiome analysis can be used to further microbial forensic technology. Future advances in this field might encompass greater sequencing depth, microbial genes beyond 16S rRNA, or inanimate objects such as glass, ceramic, or even clothing. Just as

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bloodhounds can detect the unique spoor of an individual, we can harness nucleic acid technologies and informatics to follow a microbial trail.

The work of Fierer et al. (9) leads us along an interesting new path in forensics and biology. Can changes in microbial compositions provide clues about poisonings? Could we purposefully store samples of our microbiome from saliva or stool, or in the form of our new fingerprints, to provide another level of proof of identity? Surely, such analysis will lead to new ethical dilemmas.

One important issue is whether washing or antibiotic treatments, for example, sufficiently alter our profile so that identity can be hidden or is intrinsically

unstable. Or in contrast, can we identify a core individual-specific signature that withstands such adventitious or purposeful perturbations? Just as we have an international HapMap project to understand the variation in the human genome (21), would a similarly planned project to understand worldwide conservation and diversity in the human microbiome (2) be a critical platform for future forensics? Could we also use such analysis to outline changes in the human microbiome associated with socioeconomic development (22) that might have important consequences for health and disease? In our increasingly sanitized world, can such studies help us approach the contexts in

which personal hand-sanitizers are beneficial or harmful?

More than a billion years ago, animals began domesticating microbes and allowing them permanent residence. Although we might ask who domesticated whom, we are learning how important these residents are to host survival, and how to further understand them to deepen our knowledge of personal health, identity, and social interaction. Our microbial fingerprints (9) are a fine example of our advancing knowledge.

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