

RESEARCH HIGHLIGHT

The volatile microbiome

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Abstract

The first detailed temporal study of the human microbiome shows that individual body habitats exhibit surprising variation over time yet maintain distinguishable community structures.

While the human genome is constant in an individual (except for somatic mutation), our second genome, encoded by the human microbiome, varies both within and between individuals. The microbiome is the totality of microbes that live in and on the human body, and the combined genomes of these organisms, the metagenome, produces a wealth of gene activity whose impact is largely unknown but expected to be significant. Each tissue in the body carries the same human genome in its cells, but each tissue presents a different habitat to microbes, and the microbial communities of these habitats have different compositions, and thus different metagenomes. The goal of many projects, such as the National Institutes of Health Human Microbiome Project [1], is to describe these communities, and determine the phenotype-genotype relations essential for understanding the role of the microbiome in health and disease.

The many past and present metagenomic studies of the microbiome generally do not address temporal variation, but rely on from one to a few time points for each subject or habitat sampled (for example, two to three samplings per subject for the Human Microbiome Project [1]). The most elaborate longitudinal studies to date have collected tens of samples in studies of newborns [2,3] and older people [4], or environmental shifts caused by diet [5] or antibiotic usage [6,7]. These early studies move the field in the needed direction, but await technological improvements before they can become routine elaborate experimental designs. In this issue, Caporaso *et al.* [8] make significant strides toward this realization.

Technical milestones

Caporaso and colleagues sampled three body habitats (stool, mouth and palms) from two subjects daily for 6 or 15 months, collecting hundreds of densely spaced specimens. To analyze these specimens, they used Illumina sequencing (Illumina, Inc., San Diego, CA, USA) to reduce cost and increase throughput and depth of sampling [9], and the Amazon Elastic Compute Cloud (Amazon EC2 [10]) for low cost, high bandwidth computational resources. Both of these methodologies offer the prospect of moving future metagenomic studies from the limited sampling realm to the dense sampling that may be required to decipher the patterns of the microbiome. This experimental design moves the bottleneck upstream to the sampling phase. Taking full advantage of this increased data production and computation requires more samples, and this introduces its own cost and logistics challenges.

As another technical sideline of the study, the data were a combination of sequences from different regions of the 16S rRNA gene, produced with different sequencing platforms: legacy data from 454 sequencing mixed with the Illumina 16S rRNA sequences. Sufficient concordance was observed between the data sets to allow the study to use the merged collection. There has been a prevailing concern that different sequencing methods, read lengths and variable regions within 16S rRNA perform differently in terms of the taxa they detect, so this result is of high interest for those who wish to combine data sets to increase the power of studies but are concerned about introducing biases or other confounding factors for the analysis.

Waxing and waning taxa

The picture of the microbiome that emerges from the study of Caporaso and colleagues is one of volatility. At each body site, there are relatively few taxa that are present throughout the entire sampling period. Rather, most taxa are classified as either persistent, being detectable in many consecutive samplings before disappearing, or transient, being found for only short periods of time. One has the image of the persistent organisms blooming to high numbers, only to retreat until they bloom again. All of this is amidst a flux of short-term visitors to the community.

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Another interesting characteristic is that taxa within persistent and transient categories can be different, allowing these communities to be distinguished. In the two subjects studied, the stool microbiomes of both persistent and transient communities had few predominant taxa: the Clostridia, Bacteroidia and, in one subject, Erysipelotrichi. However, the persistent and transient communities in both subjects could be differentiated by the presence of Betaproteobacteria and Deltaproteobacteria in persistent communities, while transient communities uniquely contained Gammaproteobacteria and Bacilli. In one subject, Actinobacteria, Epsilonproteobacteria and Verrucomicrobia were also unique to the transient community. The tongue and palms had many more predominant taxonomic classes, but none of these taxa clearly differentiated persistent and transient communities consistently across the two subjects.

Despite this mercurial community structure, the communities of the three different habitats remain distinguishable from each other at all times. This suggests that the players in each community, and the bounds on their abundances and half-lives, are some of the differentiating characteristics of each body habitat.

Defining disease microbiomes

It is notable that despite enormous interest and activity in human microbiome research, no associations between a disease and microbial community have been shown. Perhaps this will change once temporal variability is taken into account in experimental design and analysis. Caporaso *et al.* [8] move the field closer to being able to discern associations between microbiome structure and clinical phenotype by showing that the degree of variation over time is significant. It seems likely that this variation may provide a noise level that could obscure correlations. This does introduce a new challenge: how to analyze such temporally variable data to find robust relationships. Perhaps from this study, or future ones building on it, the number of specimens, depth of sampling, and frequency and duration of sampling needed to improve experimental designs can be deduced.

One of the hopes for making such an association is to produce new diagnostic approaches for microbiome-related

conditions. However, if long-term time series are required for these diagnoses, it will limit their utility. One hopes that within this volatile microbiome there are still unique and less variable elements to be discovered, and that these can be of use for more immediate diagnostic or therapeutic techniques.

Competing interests

The author declares that he has no competing interests.

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References

1. NIH HMP Working Group, Peterson J, Garges S, Giovanni M, McInnes P, Wang L, Schloss JA, Bonazzi V, McEwen JE, Wetterstrand KA, Deal C, Baker CC, Di Francesco V, Howcroft TK, Karp RW, Lunsford RD, Wellington CR, Belachew T, Wright M, Giblin C, David H, Mills M, Salomon R, Mullins C, Akolkar B, Begg L, Davis C, Grandison L, Humble M, Khalsa J, Little AR, *et al.*: **The NIH Human Microbiome Project.** *Genome Res* 2009, **19**:2317-2323.
2. Palmer C, Bik EM, DiGiulio DB, Relman DA, Brown PO: **Development of the human infant intestinal microbiota.** *PLoS Biol* 2007, **5**:e177.
3. Koenig JE, Spor A, Scalfone N, Fricker AD, Stombaugh J, Knight R, Angenent LT, Ley RE: **Succession of microbial consortia in the developing infant gut microbiome.** *Proc Natl Acad Sci U S A* 2011, **108**:4578-4585.
4. Claesson MJ, Cusack S, O'Sullivan O, Greene-Diniz R, de Weerd H, Flannery E, Marchesi JR, Falush D, Dinan T, Fitzgerald G, Stanton C, van Sinderen D, O'Connor M, Harnedy N, O'Connor K, Henry C, O'Mahony D, Fitzgerald AP, Shanahan F, Twomey C, Hill C, Ross RP, O'Toole PW: **Composition, variability, and temporal stability of the intestinal microbiota of the elderly.** *Proc Natl Acad Sci U S A* 2011, **108**:4586-4591.
5. Turnbaugh PJ, Ridaura VK, Faith JJ, Rey FE, Knight R, Gordon JI: **The effect of diet on the human gut microbiome: a metagenomic analysis in humanized gnotobiotic mice.** *Sci Transl Med* 2009, **1**:6ra14.
6. Dethlefsen L, Relman DA: **Incomplete recovery and individualized responses of the human distal gut microbiota to repeated antibiotic perturbation.** *Proc Natl Acad Sci U S A* 2011, **108**:4554-4561.
7. Dethlefsen L, Huse S, Sogin ML, Relman DA: **The pervasive effects of an antibiotic on the human gut microbiota, as revealed by deep 16S rRNA sequencing.** *PLoS Biol* 2008, **6**:e280.
8. Caporaso JG, Lauber CL, Costello EK, Berg-Lyons D, Gonzalez A, Stombaugh J, Knights D, Gajer P, Ravel J, Fierer N, *et al.*: **Moving pictures of the human microbiome.** *Genome Biol* 2011, **12**:R50.
9. Caporaso JG, Lauber CL, Walters WA, Berg-Lyons D, Lozupone CA, Turnbaugh PJ, Fierer N, Knight R: **Global patterns of 16S rRNA diversity at a depth of millions of sequences per sample.** *Proc Natl Acad Sci U S A* 2011, **108**:4516-4522.
10. Amazon Elastic Compute Cloud [<http://aws.amazon.com/ec2/>]

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