Human Microbiome Project: First Map of the World Within Us

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Immune disorders: The new epidemic

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Gut microbiota: health and disease

Host genetics
Mutations in NOD2, IL23R, ATG16L and IGRM

Lifestyle
Diet
Stress

Early colonization
Birth in hospitals
Altered exposure to microbes

Medical practices
Vaccination use
Antibiotic
Hygiene

Dysbiosis

Disease

Health

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The concept of “superorganism”: We=human + microbiota

- Within the body of a healthy adult, microbial cells are estimated to outnumber human cells ten to one.

Our second genome: human microbiome (genes of human normal microbiota)

The European Commission and China initiated the Metagenomics of the Human Intestinal Tract (MetaHIT) project.
Genes in the human microbiota far outnumber those in the human genome.
The goals of Human Microbiome Project

1. Characterize the microbial communities found at nasal passages, oral cavities, skin, gastrointestinal tract, and urogenital tract.

**-16S rRNA approach**

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**-Shotgun sequencing approach**: 800 bacterial strains

3. Analyze the role of microbiota in human health and disease.
The tool part I

16S rRNA analysis
Match between bacterial communities on individual keyboards and the fingers of the owners of the keyboards.
Metagenomics: obtaining genomic sequence with shotgun approach

- The majority of microbial species have never been successfully isolated as viable single strain specimens for analysis.

- A technological approach—sequencing and analysis of the genes from whole communities rather than from individual genomes.

- Allowing comprehensive examination of microbial communities, even those comprised of uncultivable organisms.

- Instead of examining the genome of an individual bacterial strain that has been grown in a laboratory, the metagenomic approach emphasizes that microbes function within communities rather than as individual species.
Shotgun sequencing

In this strategy, the DNA is first shredded into smaller fragments which can be sequenced individually. The sequences of these fragments are then reassembled into their original order, based on overlaps, ultimately yielding the complete sequence.
242 individuals were sampled across a total of 18 body sites in 5 major body regions to collect specimens for sequence analysis. Each person was sampled up to three times over 22 months, generating a total of 11,174 samples.
Timeline of microbial community studies using high-throughput sequencing

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Diversity of the human microbiome is unique to each individual, and strongly determined by microbial habitat.
Microbial taxa varies while metabolic (functional) pathways remain stable within a healthy population.
Abundant taxa in the human microbiome that have been metagenomically and taxonomically defined

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Detection of PATRIC pathogens
(the Pathosystems Resource Integration Center)

56 out of 327 PATRIC pathogens were detected in healthy individuals.
Microbial profile varies between subjects down to the species and strain level.
Strain level genomic variation enriched around genomic islands

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Reads per kilobase per million reads (RPKM)
Microbial profile and function correlates with host phenotype

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Samples collected across geography

531 samples from cities of USA, two village of Venezuela, 4 rural communities of Malawi (Amerindians)

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Differences in the microbial communities of Malawians, Amerindians and US children and adults.
Differences in the fecal microbial communities of Malawians, Amerindians and US children and adults.

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Bacterial diversity increases with age in each population
Bacterial diversity increases with age in each population

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Differences in the functional profiles of fecal microbiomes in the three study populations

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Differences in the functional profiles of fecal microbiomes in the three study populations

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Differences between family members across the three populations studied

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Pregnancy clusters vaginal microbial communities

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16S rRNA analysis reveals that the first microbiota of babies are primarily structured by delivery mode.
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Bacterial diversity of breast-fed Malawian twins and breast-fed and formula-fed USA twins

Breast-fed Malawian twins

Breast-fed USA twins

Formula-fed USA twins

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The abundance of novel reads is usually not more than 1%. The abundance of E. coli, a rare organism in human stool, is about 0.94%.
Conclusions

- Diversity of the human microbiome is unique to each individual, and strongly determined by microbial habitat.

- Pronounced differences in bacterial profile and functional gene repertoires were noted between US residents and those in the other two countries (Malawians and Amerindians).

- It matters more whether the metabolic function is present, not which microbial species provides it.

- Nearly everyone routinely carries pathogens. In healthy individuals, however, pathogens cause no disease.

- Vaginal microbiome undergoes a dramatic shift in bacterial species in preparation for birth, characterized by decreased species diversity.
Future questions

- Which factors are responsible for the day-to-day or longer-term variation in the composition and functions of a person's microbiome?

- To what degree are such factors intrinsic to the microorganisms, related to the host, or, indeed, stochastic?

- Healthy individuals carry pathogen around. Why some pathogens turn deadly and under what conditions?

- What is the basis of resilience in the human microbiome, and can it be predicted and restored?

- Westernization are changing the microbial landscape-changes that potentially mediate the immunopathological states correlated with westernization.
To alter our microbial genomes can be far easier than to alter the host genome within each of our “human” cells in order to maintain and improve health.

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Thank You and More Questions?

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