



What is the microbiome?

We humans are mostly microbes, over 100 trillion of them. Microbes outnumber our human cells ten to one. The majority live in our gut, particularly in the large intestine

The microbiome is the genetic material of all the microbes - bacteria, fungi, protozoa and viruses - that live on and inside the human body.

The number of genes in all the microbes in one person's microbiome is 200 times the number of genes in the human genome. The microbiome may weigh as much as five pounds.

The bacteria in the microbiome help digest our food, regulate our immune system, protect against other bacteria that cause disease, and produce vitamins including B vitamins B12, thiamine and riboflavin, and Vitamin K, which is needed for blood coagulation.

The microbiome was not generally recognized to exist until the late 1990s.

What does the microbiome have to do with health?

The microbiome is essential for human development, immunity and nutrition.

The bacteria living in and on us are not invaders but beneficial colonizers.

Autoimmune diseases such as diabetes, rheumatoid arthritis, muscular dystrophy, multiple sclerosis, and fibromyalgia are associated with dysfunction in the microbiome. Disease-causing microbes accumulate over time, changing gene activity and metabolic processes and resulting in an abnormal immune response against substances and tissues normally present in the body.

Autoimmune diseases appear to be passed in families not by DNA inheritance but by inheriting the family's microbiome.

Some examples:

- The gut microbiome is different between obese and lean twins. Obese twins have a lower diversity of bacteria, and higher levels of enzymes, meaning the obese twins are more efficient at digesting food and harvesting calories. Obesity has also been associated with a poor combination of microbes in the gut.
- Type I diabetes is an autoimmune disease associated with a less diverse gut microbiome. In animal studies, bacteria play a role in developing diabetes.



- Dust from homes with dogs may reduce the immune response to allergens and other asthma triggers by changing the composition of the gut microbiome. Infants who live in homes with dogs have been found to be less likely to develop childhood allergies.
- Fecal microbiota transplantation (FMT or fecal transplantation) is a clinical procedure that restores healthy bacteria in the colon by introducing stool by colonoscopy or enema from a healthy human donor. Potentially fatal *Clostridium difficile* infections (CDI) have been cured using FMT to restore healthy gut microbiota. FMT is also used to treat colitis, constipation, and irritable bowel syndrome.

What is the Human Microbiome Project (HMP)?

Worldwide research initiatives are mapping the human microbiome, giving insight into uncharted species and genes.

One initiative is the Human Microbiome Project (HMP) sponsored by the National Human Genome Research Institute (NHGRI), part of the National Institutes of Health (NIH). The HMP began in 2008 as an extension of the Human Genome Project. It is a 5-year feasibility study with a budget of \$150 million, and is being carried out in a number of centers around the US.

The purpose of the HMP is to study the human as a supraorganism composed of non-human and human cells, with the goal of describing the human microbiome and analyzing its role in human health and disease.

A major goal of the HMP is to characterize the metagenome (the combined genomes of all the microbes) of the microbiomes of 300 healthy people, over time. Five body areas are sampled: Skin, mouth, nose, colon, and vagina.

Why is the Human Microbiome Project important?

A person's microbiome may influence their susceptibility to infectious diseases and contribute to chronic illnesses of the gastrointestinal system like Crohn's disease and irritable bowel syndrome. Some collections of microbes determine how a person responds to a drug treatment. The microbiome of the mother may affect the health of her children.

Researchers mapping the human microbiome are discovering previously uncharted species and genes. Genetic studies that measure the relative abundance of different species in the human microbiome have linked various combinations of microbe species to certain human health conditions.

A more complete understanding of the diversity of microbes in the human microbiome could lead to new therapies, perhaps treating a bacterial infection caused by a "bad" bacteria by growing more "good" bacteria.

The HMP serves as a roadmap for discovering the role of the microbiome in health, nutrition, immunity, and disease.

What questions remain?

Here are some questions researchers are investigating:

- How is a specific microbiome established in an individual? Does it change over time?
- How do the human host and microbe community interact?
- How does a particular combination of microbes affect nutrition? How do changes in diet affect the microbiome?
- How does the microbiome affect immunity and contribute to disease?
- How do antibiotics affect the microbiome? Conversely, how do the microbes in our bodies affect how we respond to various drugs?
- How can a microbiome be altered to improve health?

And some related ethical issues to consider:

- Is data being collected from a representative sample of the population?
- Informed consent to collect samples
- Data sharing and protection of privacy
- Invasiveness of taking the samples
- Returning research results and incidental findings to participants

Human microbiome research also has broader societal implications:

- How will research findings be used in clinical settings?
- How will new products such as probiotics be regulated?
- How will the public understand discoveries about the microbiome?
- How could this information change conceptions of health and disease, even what it means to be human?

Food for Thought

1. What do you think about fecal transplantation (FMT) as a clinical therapy? Do you think the "yuck factor" will discourage people from agreeing to this treatment?
2. Direct-to-consumer microbiome testing company uBiome does not state what will be done with samples or data, explain how a participant's identity is protected, or share the consent form until potential participants pay \$89 for a test kit. uBiome does not have IRB oversight. What are some ethical issues around these practices, including paying to participate?
3. If you have your microbiome analyzed, you will learn how the species and abundance of microbes in your microbiome compares to other peoples' microbiomes. It is not yet understood how the composition of the microbiome relates to health. Is this information meaningful? Would you have your microbiome analyzed? If yes, what do you think would you learn?

Where to go to learn more:

The NIH Human Microbiome Project (NHGRI):

<http://www.hmpdacc.org> and

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2792171>

Human Genome 10th Anniversary: Digging Deep into the Microbiome: <https://www.sciencemag.org/content/331/6020/1008.summary>

The Microbiome and Autoimmune Disease: <http://www.ncbi.nlm.nih.gov/pubmed/23370376>

Dust in homes with dogs may protect against allergies and asthma: <http://www.ncbi.nlm.nih.gov/pubmed/24344318>

Family Ties: Taking on the intricacies of the gut microbiome, UW Medicine Center for Intestinal Microbiome Research: <http://depts.washington.edu/givemed/magazine/2013/10/report-to-donors-2012-2013/>