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A gut feeling

bugs are critical for good health

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While still in the womb, the gut of an infant is completely sterile. But as the birthing process begins, bacteria and other microbes soon start to colonize the surfaces of the infant's body—the skin, nose, mouth, and by far the most densely colonized, the gut. Babies born by caesarean section are initially populated with different microbes (from the hospital and skin microbiota) than babies delivered vaginally (vaginal microbiota) (1, 2).

During the first few years of a host's life, communities of microbes become established in it. They adapt and flourish in different parts of the body. Eventually, every human cell is outnumbered by about 10 microbial cells, and every human gene is outnumbered by about 100 microbial genes. The collective genomes of these microbes are known as the microbiome.

The microbiome performs many important functions. For example, the bacteria that line the host's intestines aid digestion and synthesize vitamins. They also protect against infection—they prevent potential pathogens from gaining a foothold. And there is growing evidence that these microbes shape the immune system. Germ-free mice, which have been raised to have intestines without bacteria, are very different than mice with a normal microbiome. Their immune systems are so poorly developed that they are extremely susceptible to pathogens.

The composition of the microbiome is shaped by many different factors. The microbes are mobile—they move between a host's body and the environment. Changes in the microbiome are associated with who lives in the same household as the host, even the presence of a pet dog. Diet also plays a role—a diet limited to processed, uncontaminated food results in a less diverse microbiome. Obese individuals have a simpler microbiome than lean people (4). And when food is scarce, evidence from animal models suggests that a "bad" microbiome may conspire with a poor diet to cause and perpetuate malnutrition (5).

Having a BLAST! Comparing DNA sequences from an obese mouse gut microbiome and a lean mouse gut microbiome against the BLAST microbial representative genomes database.

The host's gut microbiota can be disturbed by a course of antibiotics. It has been observed that infants who were given antibiotics before the age of 5 months, a time that is critical to the microbiome being established, became slightly heavier over time. By 38 months of age, they were 22% more likely to be overweight (9). Antibiotics kill harmful bacteria, but they also kill healthy bacteria, which may influence energy extraction and help keep us lean. A shift in bacterial demographics may also influence the risk of disease—from intestinal disorders (e.g., ulcerative colitis, Crohn's disease, and irritable bowel disease), to diseases such as eczema, asthma, obesity, and heart disease. Microbes may even modulate sex hormones and influence the risk of autoimmune diseases, such as type 1 diabetes (6).

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Because there are more genes in the host's gut microbiota alone than there are in the rest of the host's human body, these microbes are said to hold the "second genome". But whereas a human genome is inherited, a human microbiome is acquired—and therefore can be manipulated. If germ-free mice are given the microbiome of obese mice, they too gain body fat. This is probably because the bacteria in the obese microbiome were extracting more energy from food, thus influencing the metabolism to store rather than break down fat (7). Another study found that if young normal mice were fed with one type of bacterium, it led to an altering of those mice's brain neurotransmitters, causing changes in their behavior that are analogous to reduced levels of stress, anxiety, or depression (8).

Many of the microbes we carry have never been studied because they cannot be grown in microbial culture—they do not survive in laboratories. However, by sequencing their genomes, their genes can be studied. In 2008, the Human Microbiome Project was launched by the NIH, with the goal to identify and characterize the microorganisms that are associated with humans. It studied over 240 healthy volunteers, and took samples from five body areas or "habitats" (nose, mouth, skin, urogenital tract, and gastrointestinal tract) (10).

In total, over 5000 samples were collected, purified, and sequenced. Bacterial sequences were identified by sequencing the hypervariable regions of bacterial ribosomal RNA (16s rRNA), which contain signature sequences specific to a species. 5177 unique microbial taxonomic profiles were found. By sequencing whole-community DNA (whole genome-shotgun or metagenomic sequencing), the researchers found that while the composition of the microbes varied widely among individuals, there was remarkable functional stability. In other words, there are many ways to construct microbial communities to perform similar functions, such as aiding the digestion of lipids. Other key findings included an association between ethnicity and microbiome composition, and a correlation between vaginal pH and microbial diversity.

Now that the Human Microbiome Project has provided the first reference data for microbes living in healthy adults, the avenues for research include how these microbes fare over time—in health, disease, and treatments, from infancy to old age. Drugs may be developed to specifically target a microbiome—perhaps to aid weight loss, combat infection, inflammation, or even treat cancer.

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