The human microbiome: our second genome?

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How can two identical twins, who have the same DNA, possibly look and act profoundly differently? There are a multitude of answers to this age-old question—environmental factors, epigenetics… and we are discovering new answers every day. A particularly interesting factor to these differences is the microscopic, but essential, world of the human microbiome.

What is the human microbiome? In simple terms, it is the community of microorganisms that live on and in our bodies. But, I hear you ask, aren't microbes bad for us? Well, that is true, to an extent. Several types of microorganisms—bacteria, fungi, you name it—do cause diseases in humans. You've no doubt heard of tuberculosis, MRSA infection, salmonella, gonorrhea, and countless other deadly diseases. And you're not wrong that all these illnesses are caused by bacteria.

However, that's the occasional black sheep giving the whole bunch a bad rep. Our bodies are home to trillions of microorganisms, which inhabit almost every part of our body—from our skin to our gut. Scientists estimate that on average, there are more than 37 trillion microbes in our bodies, which far outnumbers the human cells that we have. [1] We may well be more microbe than human—and we have barely begun to scratch its surface since the term was coined in 2001.

Each and every one of us has a diverse, and unique, array of microbiota. How is this possible? Aren't we all exposed to the same microbes in our daily lives? The differences in our microbiota start even before we are born. Microbes inhabit the placenta, fetal membranes, amniotic fluid, and umbilical cord, each of which is deeply involved in development of the fetus. Microbes from the maternal gut and vagina are the sources of the newborn's first exposure to microbes.

But that's not all. The route of birth can drastically affect the microbiota that newborns are first exposed to. A natural birth exposes the newborn to the microbiota of the vagina, while a Cesarean section exposes the newborn to microbes found on the skin, mouth, and bacteria found in the operating room. These differences are not trivial—in fact, children born by Cesarean section are more likely to develop immune-related disorders such as asthma, allergies, inflammatory bowel disease, or even obesity. Some microorganisms in the microbiome can help to digest some food items that our body can't naturally make use of. And a combination of other, poorly-understood effects of the microbiome can affect our metabolism and many other aspects of our bodies in ways we're just beginning to understand.

The microbiome varies to great extents between individuals. Even though humans share 99.9% of our genomic DNA with each other, our gut microbiome can differ from other people by 80 to 90%. [1] Even our own left and right hands share less than 20% of bacterial phenotypes with each other. [2] Our unique community of microorganisms is almost like a second set of DNA—every human has a unique combination of microbes in and on their bodies.

Like our DNA or our fingerprints, our microbiome is completely unique to us; The population of our microbiome is constantly in flux. This is partially due to our natural exposure to the environment—though we might not see it, every nook and cranny of our surroundings is completely covered in all sorts of microbes. Whenever we contact the surroundings (which is basically all the time), we're exchanging our microbiota with microbes from the surroundings. Our skin, especially, has a population that fluctuates greatly because of this. In fact, it's possible to identify someone using their microbiome; researchers were able to determine who had touched a computer mouse based on the unique signature of microbiota that they left behind. And given the amount by which our microbiome differs between each person, it's not surprising that our microbiome can identify us so easily. Yet, whenever we do, the combination of microorganisms that inhabit us changes ever so slightly. Though it may seem attractive, it would be almost impossible to track a person's actions and movements in the long term just from their microbial signature. On top of the fact that the microbiome changes whenever we touch something, other microbes quickly colonize and re-colonize any exposed surface, making it almost impossible for an individual's microbiome to get a hold of a surface.

But other things we do can drastically change our population of microbiota. Taking antibiotics, for example, causes huge changes in our microbiome. Antibiotics we take usually don't discriminate between types of bacteria. And even when they do, many types of bacteria are very similar, and are exterminated indiscriminately with the rest of the pathogens invading our bodies. In fact, some types of harmful, and even deadly, bacteria are almost identical to helpful ones in our bodies. E. coli, which are often found in our gut microbiome, also has strains which cause severe diarrhea in infected people. And Enterobacteria—whose name means "gut bacteria", and rightfully, include many bacterial species found in our guts—are also on the WHO's high priority pathogens list. It's impossible to specifically target those strains with our current technology—so, any antibiotics that we use inadvertently wipe out part of our natural microbiome. Research has shown that we inadvertently begin to lose diversity in our microbiome after four days of treatment with broad-spectrum antibiotics.

But worry not—all is not lost. Our microbiome is surprisingly tenacious, and can withstand a good amount of damage and disruption. Even after a course of antibiotics, our gut microbiome is capable of rebuilding itself. The process can take anywhere from a few weeks to a few months. The extent to which the microbiome recovers differs from person to person: some people's microbiomes recover completely, while others not as well, and in many cases, some species will fail to return to the microbiome. Even then, the cutting edge of medical research is fighting this problem. The French biotech company Enterotome has been working on a new type of treatment—one that targets specific disease-causing bacteria in the gut, while keeping the rest of the human microbiome intact. What's their secret weapon? The answer lies in looking at bacterial treatment in a different way. Instead of using antibiotics to attack microorganisms, the company's new treatment focuses on inhibiting the bacteria's ability to cause inflammation in the gut by

binding to it. In this way, instead of killing the bacteria, the team's new treatment inactivates the harmful pathogens and allows the body's natural microbiome to do its job.

What does this all mean for us? The human microbiome has unlocked a whole new type of medical treatment. Chief among those is treatment of *Clostridium difficile* infection. This infection often occurs in hospitals following antibiotic treatment. One of the major reasons why this occurs is because antibiotics kill microorganisms in the gut, resulting in weakening of our microbiome, and allowing *C. difficile* to take hold easily. However, fecal transplants, in which stool from a healthy donor is transplanted into the gut of the recipient, has an 85 to 90% success rate in people with infections that have resisted antibiotics. The microbiota found in the donor's stool help to recolonize the depleted gut microbiome, allowing it to fight off *C. difficile*.

The human microbiome has a truly massive array of effects on our body that we are just beginning to understand. Some scientists think of it as our second genome, while others treat it like another of our organs. Its roles in the human body are just beginning to be unveiled, and we are learning more about it every day—definitely a stark contrast with a mere 30 years ago, when its involvement in human health was all but ignored. Who is to say what the future of the human microbiome holds?

References

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Caption

The marvelous world of the human microbiome has been unveiled to us barely 20 years ago, and we are just beginning to learn about its secrets and its integral role in our bodies. We delve deep into the microscopic world of what many scientists refer to as our second genome, and examine the exciting opportunities it presents.