Have you ever been curious to find out which microbes live inside your intestinal tract (otherwise known as your gut)? Our gut is full of microbes that are intricately connected to many physiological processes, and these communities vary between persons or as a result of changes in our diet, lifestyle or health. Changes in these microbial communities are associated with certain diseases, and the analysis of the composition of our gut microbiome can be used as a clinical tool by medical professionals.

Microbes in our gut

We humans might need a little reminder that most life on earth is microbial. It is estimated that a trillion species of microbes live on our planet, in environments such as the ocean and soil, associated with plants and animals, and also associated with us. Our bodies are home to diverse communities of microbes, called microbiotas or the human microbiome. These communities consist of bacteria, archaea, viruses and microscopic eukaryotes such as fungi that live on our skin, in our mouth, nose, stomach and gut. In fact, one of the densest populations of microbes lives in the human gut. Our distal gut harbours 40 trillion microbial cells, which is roughly the same number as human cells in our body. Most of these microbes are bacteria and together they comprise about 500 species.

Although the human microbiome is the most dense and species-rich in our intestinal tract, some other parts of our bodies that are exposed to the outside are home to microbial communities as well. Our skin is covered with a thin layer of bacteria, our mouths and noses each have their specialized microbial inhabitants and most healthy vaginas are colonized by Lactobacillus species. In addition to this variation per anatomical site, these microbiomes differ from person to person, even among healthy subjects.

The microbes in our gut are essential for human health. They digest dietary components that are indigestible by human enzymes, make vitamins and other molecules needed for our physiology and help protect us against pathogens. Interestingly, our gut microbes can vary over time as well, as they respond to the food we eat, changes in environment during travel, antibiotics we take, fluctuations in our health and as we age.

The composition of the gut microbiome has historically been sampled by collecting, transferring and delivering full stool samples to laboratories which use traditional techniques to culture bacteria. Stool is the end product of a six-metre journey of food remnants, fermentation products and gut microbes that continuously divide and grow, but inevitably end up in the toilet bowl. It can also be used to monitor our health, by analysing its colour, consistency, presence of blood, or the presence or absence of pathogens and beneficial bacteria.

Impressive developments in DNA sequencing technologies have improved the high-throughput analysis of large numbers of samples, including gut microbiome samples from stool. The microbes present in stool or other types of samples can now be analysed using genetic techniques that directly amplify and sequence the bacterial, archaeal, viral and fungal DNA without having to culture them on a Petri dish. These developments have greatly enhanced our knowledge about the composition and functions of human-associated microbiomes.

Gut microbes in health and disease

Since our gut microbiome is so intricately connected to our body, our diet and our health, it is not surprising that many gastrointestinal diseases are associated with changes in its composition. By comparing stool samples from patients with health conditions, for example Crohn’s disease, ulcerative colitis, colorectal cancer or diabetes, to those from healthy people, researchers have found bacterial signatures associated with these diseases. Certain bacterial groups such as Akkermansia, Bifidobacterium, Blautia, Butyrivibrio, Eubacterium, Faecalibacterium, Prevotella, Roseburia and Ruminococcus are present in the stool of most healthy individuals, with decreased relative abundance in the stool of people with gastrointestinal disorders. In contrast, other bacterial groups such as Escherichia, Desulfovibrio, Dialister and Fusobacterium are increased in individuals with intestinal diseases.

It is worth pointing out that associations between the relative abundances of gut microbial species and diseases are just that – associations. They simply tell us...
that the gut microbiome in patients is different from that of healthy people, but such associations cannot distinguish between cause and effect. In addition, it is often hard to tease apart the combined effects of diet, health condition, medicine use and gut microbiome composition. For example, Crohn’s disease patients are likely to have a recent history of medicine use, and often exclude certain food items that trigger exacerbations in their diet, both of which might already influence the composition of their gut microbiome. In another example, people who eat a lot of red meat might have a higher risk of atherosclerosis, so the finding that gut bacteria in patients with that disease are different from those in healthy controls might just be the result of eating a different diet. However, in this particular case, there is scientific evidence that the gut microbiome is indeed directly involved, because gut microbes can convert carnitine, a molecule in red meat, into molecules involved in atherosclerosis.

Recent studies have also greatly increased our knowledge about the molecules that each of these bacterial groups make. *Blautia, Eubacterium, Faecalibacterium* and *Roseburia*, for example, break down dietary fibres and produce butyrate, a short-chain fatty acid. This small molecule serves as fuel for intestinal cells, and might be one of the key signals connecting our gut to other organs including our brain. *Oxalobacter formigenes* degrades oxalate, a molecule involved in the formation of calcium-oxalate kidney stones. People whose gut microbiome contains *O. formigenes* might therefore have a lower risk of kidney stones than people lacking this bacterium in their gut.

**Analysing your own microbiome**

With more and more mainstream media articles about the important role of the gut microbiome in our health, it’s not surprising that people are curious about the composition of the microbes in their own gut, if it falls into a healthy range and what they can do to improve their health. Microbiome analysis, however, was until recently only performed in academic research centres. To make such tools available for the general audience, uBiome, a San Francisco-based start-up provides a platform that turns the public into ‘citizen scientists’ to answer questions about their own microbiome. The uBiome Explorer™ kits allow people to analyse their own microbiome from different sites (such as gut, mouth, nose, skin or genitals) and track their responses to different lifestyle changes such as diet, exercise, travel, etc. uBiome Explorer users can learn more about their microbiome and how their samples compare with others in the world’s largest microbiome database with nearly 150,000 samples.

**Microbiome analysis at the doctor**

Given the rapidly increasing list of health conditions associated with a disturbed gut microbiome, analysis of the composition of the microbes present in stool samples is likely to become a part of regular healthcare. Taxa detected in the gut microbiome include many bacterial groups associated with health or disease.
In 2016, uBiome released SmartGut™, the first sequencing-based clinical microbiome screening test that determines the relative abundance of microbial groups in patients’ stool. This is the first test that determines ranges of these microbes – similar to those performed on blood samples, such as cholesterol, iron, haemoglobin, etc. – based on a healthy cohort of nearly 900 people.

As a doctor-ordered, insurance-reimbursed test, SmartGut™ enables doctors direct access to uBiome’s CLIA-certified, CAP-accredited laboratory and bioinformatics. The laboratory processing is highly automated and the data analysis is performed by a bioinformatics pipeline that processes and interprets the sequence data. Analysed data made available in one clinical report gives doctors a clear picture of patients’ overall gut health – including information on specific pathogens and microbial diversity – with documentation on how to interpret the data with supporting scientific publications. Additionally, sampling methods used by uBiome greatly reduce the sampling burden on behalf of the patient – one simply swabs stool from a piece of toilet paper, stirs in a small vial and returns to the laboratory in a pre-paid envelope.

As more and more diseases are linked to the status of the gut microbiome, stool analysis by the doctor is likely to play an increasing role in diagnostics and patient care. uBiome’s clinical test offers medical professionals a welcome additional tool in the diagnosis and treatment of many chronic health conditions.

**Precision DNA sequencing™ technology**

Metagenomic deep-sequencing is often used in identifying microbial pathways, novel functional genes, antibiotic resistance genes and genes involved in interactions and coevolution between the microbiome and host. However, deep sequencing is unable to easily resolve low abundance species or genes. To overcome this limitation, uBiome launched the SmartBiome™ platform in 2016. SmartBiome™ uses a combination of full metagenomic deep-sequencing and the simultaneous specific enrichment and identification of additional targeted genes of agnostic-type samples, a platform based on a pioneer patent-pending method termed precision DNA sequencing™. SmartBiome ID™ for infectious disease is the first product on this platform, providing hypothesis-free detection of hundreds of bacterial, viral, fungal and eukaryotic targets from a single sample of a variety of types, including blood, stool and urine, among others.

**The future of microbiome analysis**

Microbiome research is an exciting field with enormous possibilities for our health. The development of the technologies described above has already led to a better understanding of the microbes present in health and disease, and is expected to result in new diagnostic tests and therapeutics in the near future. Collaboration between academic centres and industry might be as beneficial as the symbiosis between our microbial communities and our bodies.

uBiome will continue to build on its research capabilities and develop broad-spectrum clinical microbiome tests with unprecedented precision. uBiome has a successful record of diverse collaborative studies including work with the Centers for Disease Control (CDC) to better understand hospital-acquired infections, a project with Harvard University on a large-scale study of the relationship between genomic and microbiome data in collaboration with Dr George Church, and investigations with the University of North Carolina that aim to better understand the relationship between the microbiome and eating disorders.

It is beyond doubt that these and other collaborations will lead to valuable new insights in how our microbiomes affect our health, and new ways to improve our health by changing their composition.

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**Further reading**