

Revealed: the 160 species living inside our guts

Scientists have decoded the DNA of the bacteria that take up residence in the typical human gut.

Some scientists dream of sending a probe to Mars, others work on ways of exploring the sea with robotic submersibles. Now a team of researchers have boldly gone where no human has before – they have decoded all the bacterial genes found in the human gut.

It may not have quite the same cachet as space exploration or marine biology, but the detailed examination of what is living inside each and every one of us is nevertheless likely to have far-reaching implications for human health and wellbeing, and could even be used to predict chronic intestinal illnesses, from ulcers to cancer.

The study decoded the DNA sequence of the many thousands of genes used by the vast number of bacteria which take up permanent residence inside the human intestines. It found that about 160 different species of microbe can live in the healthy human gut and that each person on average has about 160 species living inside them at any one time – and most of these species are common to different people.

Studying gut bacteria has been difficult, because many are unable to be grown outside of their natural habitat, which is why the scientists believe their findings will shed light on a little-understood or discussed aspect of human biology.

It is estimated that a healthy human gut contains about 100 trillion microbial cells, about 10 times as many cells as there are in the human body. Yet next to nothing is known about what these bacteria do to maintain health and wellbeing, said Jeroen Raes of Vrije University in Brussels, a member of the international team which decoded the gut genome.

"We have no clue as to how the gut works because this is a very complex ecosystem. We don't know how that ecosystem works even though it is crucial for our wellbeing. We don't know how food is digested and which species do what," Dr Raes said.

"We've basically sequenced all of their genomes at once. It was a huge effort because it's by far the biggest sequencing exercise anyone has done so far – it's about 200 times the sequencing effort of the human genome project," he said.

The scientists took faecal samples from 124 Europeans and analysed the DNA they contain using powerful "gene machines" that could quickly decipher the order of the genetic "letters" along the length of each DNA molecule, the unit of inheritance.

They used a technique called metagenomics, which attempts to sequence every scrap of DNA in a scrambled sample without first having to isolate each and every microbial species. With the sequences it is possible to work backwards to estimate how many microbial species are present, said Jun Wang of BGI-Shenzhen in China, one of the world's biggest genome research centres.

"From all the genes in the human gut, over 99 per cent of them are bacterial, indicating that the entire cohort harbours between 1,000 and 1,150 prevalent bacterial species and each individual person has at least 160 such species, which are largely shared [from one person to another]," Wang said.

"Our intestine is home to our largest collections of microbes. Bacterial densities in the colon [large intestine] are the highest recorded for any known ecosystem... the surprise has been the genetic diversity of the microbes correlated so well with human health. We have to really study the 'other genome'."

ourselves."

Dr Raes said the study, published in the journal Nature, was a technical tour-de-force because it involved the simultaneous mass screening of so many different kinds of microbes, some of which are new to science and have never before been studied.

"We've used this novel DNA sequencing technology to build a big map of all of the genes of the bacterial flora in our gut. We found about a 1,000 species of bacteria and we hardly know what they are and we definitely don't know what they are doing," Dr Raes said.

"It was very surprising for us to find that we have so much more in common than we thought we had. The guts of different individuals have a substantial overlap in terms of species composition and function because it was always thought that human gut flora was very variable."

The human gut is effectively sterile until birth and in the first year of life the flora fluctuates a lot but it begins to settle down after weaning. It is clear from research on laboratory animals that a diverse mixture of gut bacteria is essential for digestion and some medical authorities believe that probiotics may help to fend off disease.

"This blueprint helps us to see the natural variation in healthy individuals. But it also has a clinical component in that we also see that for people with Crohn's disease or ulcerative colitis we can already separate them based on their gut flora... we may be able to predict whether someone is susceptible to these diseases," Dr Raes said.

"This study is like the first blueprint. We are gathering all the pieces as it were and we're starting to piece them all together. We are not there yet but now we use this information to compare healthy individuals with patients with Crohn's disease or ulcerative colitis, or with obese people," he said.

The human gut is just one "ecosystem" being targeted by the technology of metagenomics. Environmental biologists are also sampling seawater in the same way, to see what kind of bacteria and other microbes can be found there. Like the investigation of gut bacteria, scientists are discovering a vast array of hitherto undiscovered microbes.

"A lot of things we found were new... whenever you go fishing for microbial diversity you find thousands of novel species because the microbial world is vastly uncharted," Dr Raes said.

"It's a technical tour-de-force. It was not thought we could do metagenomics on this scale... it's a snapshot for a single moment for each of these individuals, so we know we have an idea about the variation among individuals, but we have no idea about change over time."

The next stage is to see how the composition of gut flora varies during a person's lifetime at different stages of a disease, and to see whether there are significant differences between ethnic groups in different regions of the world.