MedicalXpress

Researchers develop tool to understand how the gut microbiome works

March 11 2015

Researchers at Harvard Medical School and Columbia University in the United States have developed a way to study the functions of hard-to-grow bacteria that contribute to the composition of the gut microbiome. The new method is published in the journal *Molecular Systems Biology*.

"Our method, TFUMseq, is a powerful tool for understanding how the wealth of microbes that we harbour in our bodies are so successful at colonizing us. It provides a general high-throughput approach to identify genes that enhance the fitness of microbes over time as they grow in complex living organisms," says Georg Gerber, one of the lead authors on the study, and Assistant Professor at Brigham and Women's Hospital at Harvard Medical School.

Most of the genes in the human body do not come from human cells but are found within the trillions of microbes that live on or within the human body, particularly in the gut. Working out the functions of these microbial genes is a big challenge because many of the microbes that live within us are extremely reluctant to grow when cultured under laboratory conditions.

The new method circumvents the problem of not being able to culture many of these bacteria in the lab by transferring genes from these bacteria into another bacterial species that is easier to work with. It is then possible to look for tell-tale signs of advantages conferred to the recipient bacterial species as it grows in the mammalian gut over time.

In their demonstration, the researchers used the bacterium *Bacteroides thetaiotaomicron*, a microbe that lives in the human intestinal tract, as their "donor organism," that is the one whose functions they wanted to study in more detail. The more manageable recipient was *Escherichia coli*, which can be easily manipulated in the lab. *E. coli* organisms harbouring fragments of DNA from the "donor organism" were then fed to germ-free mice, which are animals that are raised in special environments (isolators) that prevent the entry of any bacteria.

The scientists were able to use the method to uncover improvements in the capabilities or fitness of the recipient *E. coli* bacteria growing in the mouse gut that were due to characteristics being passed on from the source bacterium. In particular, they detected *E. coli* organisms that were being selected due to their improved abilities to use different carbohydrates as a source of energy, a property conferred by the source bacterium *B. thetaiotaomicron*.

The work is the first time that a large-scale functional genomic approach has been used to systematically examine how bacteria can gain capabilities that improve their ability to colonize living organisms, in this case mice. The work also allows building up a picture of the behavior of different genes of the gut bacteria over time, so-called kinetic information. This information provides clues as to when different genes are most important during the complex process of colonizing a living organism.

Harris Wang, a lead author on the study, and Assistant Professor at Columbia University, added: "The use of the TFUMseq approach could allow the rational design of bacterial strains for various clinical applications, for example improving the ability of probiotic bacteria to colonize the gut, resisting colonization by pathogens, compensating for unbalanced diets, such as too much fat or sugar, or improving the function of the immune system to prevent diseases."

More information: msb.embopress.org/content/11/3/788