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Tell me what you eat and I will tell you how your microbiota evolves

New study reveals how gut bacteria adapt and affect health in response to diet

Oeiras, 26th January 2022 – New research reveals that diet can change the evolutionary path of bacteria in the gut, within host-relevant timescales. The study, published in *Cell Host & Microbe*, demonstrates how quickly *Bacteroides thetaiotaomicron* (*B. theta*), a prevalent bacterium in the human gut, acquires adaptive mutations in response to dietary changes. These findings show that acquisition of genetic changes can explain the observed microbiota-mediated negative effects that unbalanced diets have on host health.

Our gut is inhabited by a diverse community of microbes, the gut microbiota. This community, composed of hundreds of different species, is essential to our health: it influences our immune system, protects us from infections, and helps us digest food. However, many factors, such as drugs, inflammatory responses to infections, and lifestyle can perturb the composition of the microbiota and decrease its diversity, often leading to disease.

Several gut bacteria, including *B. theta*, rely on dietary polysaccharides (complex carbohydrates formed by long chains) from plant fibers for their functions. Nevertheless, in the context of a low-fiber diet, *B. theta* can change its gene expression and metabolism to degrade polysaccharides from its host's gut mucus instead. By decreasing the thickness of this protective layer, this shift increases the host's susceptibility to infection and inflammation.

Diet is known to cause microbiota imbalances underlying a variety of pathological conditions, however, the effects of low-fiber Western-style diets on bacterial evolution remain unexplored.

New experimental data from the Instituto Gulbenkian de Ciência (IGC) revealed that, in addition to gene/metabolic regulation, the emergence of adaptive mutations in response to dietary changes can also influence and shape microbiota function. This new study followed the evolutionary dynamics of *B. theta* in mice that were either kept on a standard diet, rich in microbiota-accessible carbohydrates (i.e., plant fibers) and low in fat and simple sugars, or a Western-style diet, rich in fat and sugars but poor in fiber.

The authors observed that *B. theta* evolved rapidly in the murine gut, accumulating diet-specific adaptive mutations within a couple of weeks. While bacteria in mice on a standard diet acquired mutations that promoted fiber degradation, bacteria in mice fed a low-fiber diet accumulated mutations that favored the degradation of the host's mucus, demonstrating that these microbes evolve and adapt to distinct gut environments generated by dietary change. Importantly, since they reflect the host's diet, these emerging mutations could be used as a biomarker of dietary differences between individuals.

The study also included a group of mice that underwent weekly changes from standard to Western diet. These periodic shifts led to rapid fluctuations in *B. theta*'s genetic and metabolic signatures, resulting in the maintenance of a higher genetic diversity compared to constant dietary regimens. According to Tanja Dapa, IGC researcher and first author of the study, these results suggest that periodic variations in diet, for example, through supplementation, might be

important to avoid the fixation of specific mutations and to maintain a high genetic diversity in the members of the microbiota.

Taken together, these findings emphasize that gut bacterial evolution is an important mechanism involved in shaping microbiota function, with more permanent consequences than that of gene regulation. Such information could improve our understanding of microbiota-dependent host responses to diet and to other perturbations, including the use of antibiotics. “The consequences of an unbalanced diet can be much more permanent than previously recognized because diet affects not only the composition of the microbiota, but also leaves permanent genetic alterations in the gut microbes. Although not addressed in this study, our results indicate that these alterations can be transmitted to the next generations, thus having long-lasting consequences”, reinforces Karina Xavier, leader of the IGC group responsible for the research.

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