

21 August 2019 | **Bacterial sex drives evolution of microbes to conquer and colonize the gut**

In a pioneer study now published in *Proceedings of the National Academy of Science – USA*, the research team led by Isabel Gordo, from the Instituto Gulbenkian de Ciência (IGC) (Portugal), in collaboration with researcher Michael Lässig of Cologne University (Germany), used healthy mice to study real-time gut colonization and discovered a pivotal role for bacterial sex in the evolution of the mammalian microbiome. This discovery constitutes a paradigm shift and opens the possibility to design phage-targeted therapies capable of dealing with the aftermath of infection and antibiotic usage, as well as antibiotic-resistant bacteria.

Most of what we know about bacterial colonization of the gut comes from studies with pathogenic bacteria in highly artificial laboratory models or disease contexts. Standard experimental models, which focus on infections with pathogenic bacteria and continuous antibiotic treatment, have not detected phage-driven horizontal gene transfer (HGT) and suggest that bacteria colonizing the gut evolve mainly through accumulation of mutations. In a surprising finding, the work of the IGC researchers now shows that HGT, not mutations, is the first evolutionary mechanism driving the pace and outcome of bacterial evolution in a healthy gut.

Escherichia coli is a common colonizer of the human intestine as well as a potential pathogen. The colonization outcome is greatly influenced by different speeds and modes of evolution of this opportunistic bacterium. *E. coli* can evolve through mutations, which are then inherited by daughter cells, or through a process of recombination, i.e. bacterial sex, in which genetic material is shared between unrelated individuals. In the mouse and human intestine, this transfer of genetic material involves temperate bacteriophages (phages), viruses that infect bacteria and integrate into the bacterial chromosome as prophages, a process called lysogeny. Prophages can later extricate themselves (and their genetic information) from the bacterial DNA and infect other bacteria in the gut microbiome.

Nelson Frazão, a post-doctoral researcher in Isabel Gordo's lab and junior author of the study, says: "phages often classified as selfish particles reveal their altruistic side in the gut, providing a metabolic advantage to their bacterial host to conquer and colonize the gut". The phage genetic material that is transferred enables bacteria to gain access to specific carbon sources present in the gut, which provides a fitness advantage to phage-carrying (lysogenic) invader bacteria.

"We found that the classical evolution model does not apply, and in fact horizontal gene transfer greatly overrides the contribution of evolution through accumulation of

mutations in the intestine of a healthy mouse", says the investigator Isabel Gordo. "With this work, we now understand better how evolution works in normal, healthy hosts", says Nelson Frazão, junior author of the publication.

The work was conducted at the Instituto Gulbenkian de Ciência in collaboration with Cologne University (Germany). This work was funded by the Portuguese Science Foundation (PTDC/BIA-EVF/118075/2010), the Deutsche Forschungs-gemeinschaft (grants SFB 680 and SFB 1310) and a Global Grant for Gut Health-623877.

Paper: Frazão, N., Sousa, A., Lässig, M., Gordo, I. (2019). Horizontal gene transfer overrides mutation in *Escherichia coli* colonizing the mammalian gut. PNAS.

About the Instituto Gulbenkian de Ciência

The Instituto Gulbenkian de Ciência (IGC) is an international research institute, based in Portugal, devoted to biological and biomedical research, innovative training and embedding "science in society". The IGC was established by Calouste Gulbenkian Foundation, a private charitable foundation promoting innovation in charity, arts, education and science. IGC's mission is to pursue frontier research underlying both organism health and its interaction with the environment, to incubate future leaders and to place science at the heart of society.

The IGC hosts international and multidisciplinary research groups, providing them with state-of-the-art research facilities in a stimulating, cooperative and autonomous environment. At IGC there are several ambitious graduate training programs and a dedicated program to promote "science from all for all": science open to society and to talent from everywhere in the world.

For more details contact:

Ana Morais
Head of Institutional Communication
@: anamorais@igc.gulbenkian.pt
Telm.: +351 965 249 488