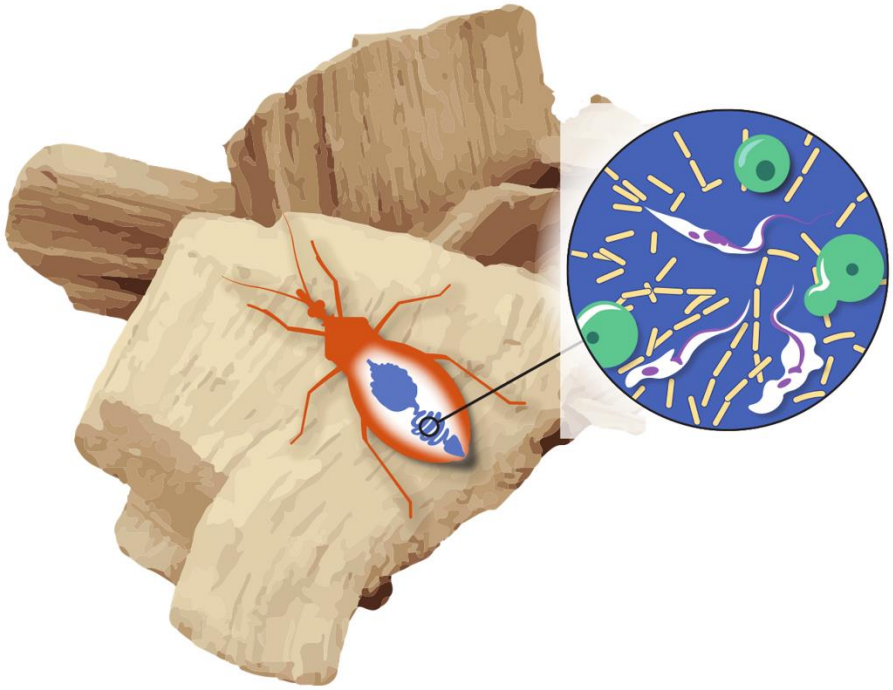
Microbes in the gut of triatomine bugs can negatively affect the growth of *Trypanosoma cruzi*.

Chagas disease is an endemic zoonosis in Latin America, and it is mostly concentrated in rural and poor areas. It is considered a neglected tropical disease, and the main vector in Central America is *Triatoma dimidiata*. With the hypothesis of microbial compartmentalization in the different gut sections, we investigated the interaction of *Trypanosoma cruzi* and the microbes inhabiting the gut of T. dimidiate, using metabarcoding and culture dependant methods. The metabarcoding approach, based on 16S rRNA sequencing, showed very similar results to previous reports and could not conclude differences related to the different sections of the gut or the infection status in the triatomines. However, the functional analysis of isolates showed ecologically relevant interactions. Different from traditional studies on triatomine bugs linking microbes to nutritional associations, we concluded that highly abundant bacteria in the gut of *T. dimidiata* show a secreted and constitutive effect that significantly inhibits the growth of T. cruzi. These bacteria in genera *Brevibacterium* and *Tsukamurella* (phylum Actinomycetota), were not the only isolates showing inhibition of the protozoa. We also recorded such effect by yeast isolates in the genus Candida, an effect even more inhibitory than a positive control using benzimidazole. Moreover, the microbes with an anti-protozoan effect did not inhibit the growth of other bacteria and fungi tested, and the effect was also different between strains of *T. cruzi* even within the same genotype (TcI). We highlight that further research on the microbial and chemical ecology in the gut of triatomine bugs may help to develop new treatment strategies and improve current control efforts, impacting the way we manage Chagas disease.

A multipartite chemical warfare occurs in triatomines…



… a successful infection also means that *Trypanosoma cruzi* overpass the antimicrobial effect of gut microbes.