Title: **The human fecal metabolome modulates *Salmonella enterica* motility gene expression**

Authors Alves, E.S.[1], Pegado, E.I.B.[2], Pina, L.C.[2], Rego, A.M.[2], Silva, D.A.[2], Ferreira, R.B.R.[1], Lobo, L. A.[1], Domingues, R.M.C.P.[1], Antunes, L.C.M.[2]

Institution [1] UFRJ - Universidade Federal do Rio de Janeiro (Avenida Carlos Chagas Filho, 373 - Rio de Janeiro, RJ), [2] FIOCRUZ - Fundação Oswaldo Cruz (Estrada da Curicica, 2000 - Rio de Janeiro, RJ)

Abstract:

The human gastrointestinal microbiota is an intricate assembly of microorganisms, estimated to contain over 1000 species, and that has critical functions for the maintenance of host health. Current knowledge of the gastrointestinal microbiota and its relationship with the host suggests that complex interactions between different microbial species as well as between microbes and host cells occur in this environment. Such interactions have the ability to affect not just the relationship between the cells involved, but may also impinge on host resistance or susceptibility to invasion by exogenous pathogens. In order to better understand the interactions between the microbiota, pathogens and the host in the gastrointestinal tract, we studied the effect of small molecules produced by the gastrointestinal microbiota on *Salmonella enterica* serovar Typhimurium. Initially, the effect of a crude extract of human feces on *Salmonella* growth and gene expression was studied. This revealed that *Salmonella* readily responds to the presence of intestinal small molecules. Several genes were regulated by the extract, and its effect on genes involved in host cell invasion was thoroughly described in previous work. Here, we show that the expression of genes involved in motility was also highly modulated by the fecal extract. Previous results using RNA sequencing and a fecal extract from an infant demonstrated an inhibition of motility genes of *Salmonella* by a fecal extract. Interestingly, when we tried to reproduce these results using feces from two adults we observed the opposite phenotype, with motility genes being upregulated. Further studies will be required to generate a better understanding of the microbiota activity involved in these results. We have previously shown that a certain commensal, *Clostridium citroniae*, was responsible for the bioactivity against invasion genes in *Salmonella*. Additionally, our previous work has shown that a specific metabolite from the gut metabolome, 3,4-dimethylbenzoic acid, inhibited invasion gene expression. Current studies are now addressing whether *C. citroniae* and 3,4-dimethylbenzoic acid are responsible for the regulation of motility genes elicited by the fecal extracts. This work deepens our previous knowledge of the roles of the human gut microbiota and provides a framework for the study of other small molecules involved in microbiota- pathogen interactions.

Keywords: *Salmonella enterica*, signaling, microbiota, small-molecules.

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