TITLE: ACTIVITY OF THE HUMAN GUT METABOLOME ON *Vibrio cholerae* VIRULENCE GENE EXPRESSION

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ABSTRACT:

Humans live in symbiosis with a diverse community of microorganisms, the composition of which has evolved to carry out many specific tasks that benefit the host, including the digestion of food, production of end-products that are taken up by the host, production of key vitamins and hormones and development of the immune system. Within the chemical diversity of the gastrointestinal tract, many of the molecules found could constitute important chemical cues for the communication between the gut microbiota and invading pathogens. Furthermore, the intestinal microbiota may have evolved protection mechanisms against pathogens by producing molecules that could modulate their virulence mechanisms. The goal of this work was to investigate the production of molecules by the human intestinal microbiota that presented biological activity against the human pathogen *Vibrio cholerae*. In order to probe the unknown functions and properties of the human gut metabolome, we extracted molecules from fresh feces of a healthy donor using ethyl acetate, allowed the solvent to evaporate and tested the effect of the dried extract on *V. cholerae*, comparing bacterial growth in the absence and presence of the fecal extract. In these experiment, we observed that the molecules present in the fecal metabolome can inhibit the growth of *V. cholerae*, although the exact reason for this effect is still unknown. The next step was to determine if the fecal extract could modulate the expression of virulence-related genes. Expression analysis by quantitative PCR revealed that the presence of molecules from the fecal extract significantly repressed at least four genes related to *V. cholerae* virulence (*ctxA, ctxB, zot, tcp*). We are currently performing RNA sequencing to further investigate the effect of the fecal extract in the global gene expression profiles of *V. cholerae*. Our results show that some of the small molecules present in the gut metabolome have a significant impact on the microbe-microbe interactions established in this environment and provides a framework for the study of other small molecules involved in microbiota-pathogen interactions. Future work will reveal new molecules in the intestinal environment that are involved in interspecies interactions and which may have potential antivirulence activity that can be pursued for therapeutic purposes.

Keywords: *Vibrio cholerae*, signaling, microbiota, small-molecules.

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