DEVELOPMENT OF A PARATRANSGENIC LUTZOMYIA *LONGIPALPIS* BY ENGINEERED BACTERIA DRIVING REFRACTORINESS TO *LEISHMANIA INFANTUM* INFECTION.

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The parasite *Leishmania infantum* is the etiologic agent of American visceral leishmaniasis (AVL), a neglected disease transmitted by the sandfly *Lutzomyia longipalpis*. The current scenario of territorial expansion with increasing incidence and lethality of AVL highlights the need for new strategies to control the spread of this disease. Paratransgenesis is an approach, in which symbiotic bacteria of insect vectors are engineered to drive antiparasitic molecules and reduce their vectorial capacity. The aim of the present work is to select molecules with anti-leishmanial activity to produce a paratransgenic sandfly to block *L. infantum* transmission. To select an effector molecule, we used the MTT assay to test the cytotoxic effect of 6 antimicrobial peptides (AMPs). Artificial infection experiments were performed to assess the AMP effect on parasite load and sandfly fitness. We determined that 16μM of the AMP-3 was toxic to *L. infantum* in axenic cultures and artificially infected *L. longipalpis* females, but had no deleterious effects on the vector. To establish a delivery system for the AMP in the vector, bacteria from the gut of female *L. longipalpis* were isolated after blood feeding, identified by sequencing the 16S rRNA, and tested for hemolytic activity and resistance to AMP. We selected an *Escherichia* sp. non-sensitive to this AMP and genetically modified with a plasmid for constitutive expression and signal peptide-mediated secretion of AMP. This plasmid was electroporated into bacteria and AMP secretion and their activity was tested through Dot Blot and MTT assay. We observed that the conditioned media from the transgenic bacteria was able to reduce the *L. infantum* axenic culture viability. Our next steps include testing these transgenic bacteria effects on parasite viability during their development in *L. longipalpis*. In this way, we propose the development of a paratransgenic sandfly with reduced vectorial capacity to transmit the *L. infantum*.

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Lutzomyia longipalpis; Leishmania infantum; Paratransgenesis.