IDENTIFICATION AND TESTING OF CANDIDATES FOR THE DEVELOPMENT OF LEISHMANIASIS TRANSMISSION BLOCKING VACCINES

Vinicius Wakoff Fonseca[1], Thais Lemos-Silva[1], Eduardo Fonseca Pinto[2], David L. Sacks[3], Yara Maria Traub-Cseko[1]
[1]Laboratório de Biologia Molecular de Parasitas e Vetores, Instituto Oswaldo Cruz, Fiocruz, Rio de Janeiro - RJ - Brasil; [2]Laboratório Interdisciplinar de Pesquisas Médicas, IOC, FIOCRUZ-RJ, [3]Department of Laboratory Medicine, National Institutes of Health, Bethesda - US.

American visceral leishmaniasis (AVL) is considered a major neglected public health problem. There has been a significant increase in the number of human cases of visceral leishmaniasis in recent years, which in Brazil is caused by *Leishmania infantum chagasi*, transmitted by *Lutzomyia longipalpis.* There is a demand for new approaches in the control of leishmaniasis due to the lack of vaccines and limitations in the use of traditional vector control methods, such as insecticide resistance, costs, etc. An alternative strategy for controlling this disease is the use of transmission-blocking vaccines (TBVs), which consist of immunizing vertebrate hosts with vector or parasite antigens responsible for establishing the pathogen in the vector, thus stimulating the production of neutralizing antibodies that will interrupt the development of the parasite inside the vector, blocking transmission. We are working with several promising candidates in the parasite, both by testing insect infection with mutant parasites (either obtained through collaborations or by creating mutants through CRISPR) and performing artificial infections in the presence of antibodies against proteins of interest. Our group identified potential targets for TBVs in *Leishmania*, which may be essential for its development in the insect. Among them are LFR1 and LIT (related to iron metabolism), ATP11 and ABC (transporters of amino acids and other molecules, respectively) and a chitinase, which appears to play an important role in the transmission of Leishmania by the vector. We produced *Leishmania* chitinase mutants by CRISPR that were 100 times less efficient than controls in artificial transmission assays. From the identified targets, synthetic peptides were designed and inoculated into mice or rabbits, in the presence of different adjuvants. Finally, artificial infections of *L. longipalpis* with *L. i. chagasi* were performed in the presence of the sera. Initial results show promising results with the decrease of parasite load in insects infected in the presence of the immune sera.

Inova-Fiocruz, FAPERJ, INCT-Entomologia Molecular

Keywords: Leishmania, sandfly, transmission blocking vaccines.