TOWARDS MOLECULAR TARGETS FOR EPIDEMIOLOGIC STUDIES OF LEISHMANIASIS

Author(s) Elisa Cupolillo, Renato Porrozi, Patricia Cuervo, Mariana Boité, Gabriel Eduardo Melim Ferreira, Grazilele Cardoso da Graça, Barbara Neves dos Santos, Davi Coe Torres, Taise Salgado de Oliveira

Institution(s) 1. Fiocruz, Fundação Oswaldo Cruz, Av Brasil 4365, Manguinhos, RJ, 21045-900

Abstract:

Leishmaniasis is a disease caused by a polymorphic group of protozoan parasite classified in the genus *Leishmania*, which are associated with several vertebrate and invertebrate hosts. Many species and their genetic variants are capable of producing a variety of clinical manifestations. Considering the public health importance of leishmaniasis in Brazil and the role of the genetic polymorphism of the parasites in the epidemiology of the disease we have developed/applied molecular markers aiming to analyze the genetic variability of this parasite and to correlate this with eco-epidemiological features. Using molecular markers, we have defined the *Leishmania* species that are circulating in many Brazilian endemic regions, associating species/strains with a particular transmission cycle. Proteomic approach was carried out and indicates that *Leishmania* promastigotes secrete proteins involved in immunomodulation, signal transduction, and intracellular survival, such as HSP70, acid phosphatase, activated protein kinase C receptor, elongation factor 1β, and tryparedoxin peroxidase. We observed DNA sequence polymorphisms in genes encoding proteins related to antimony resistance (AQP1, hsp70, MRPA and TRYR). It was observed a lower nucleotide diversity in the treatment failure isolates in comparison to those from cured patients. Based on a multiple logistic regression model, a significant therapeutic failure increase was observed among *L. braziliensis* isolates when there was a guanine instead of an adenine at position 1735 of the hsp70 gene. Using microsatellite analysis, we detected a lower heterozygosity (mean Ho=0.015) than expected (mean He=0,180) in *L. infantum*, indicating high prevalence of inbreeding, that is supported by mean FIS. Clustering method and FST indicate strains grouping in two populations. Structure in Brazilian *L. infantum* populations does not seem to be geographically related. Multi-locus sequence analysis using housekeeping genes are also being conducted by our group. We have analyzed the *L.(Viannia)* subgenus by sequencing the enzyme-coding genes MPI, ICD, G6P and 6PG. Polymorphisms were detected as well as species specific alleles. Heterozygotic samples were identified. These studies generate a new outlook on *Leishmania* and provide a solid basis for new generation genome based molecular epidemiology studies.

Key words: Leishmaniasis, MLST, molecular epidemiology