

Adaptation of *Leishmania donovani* to Cutaneous and Visceral Environments: in Vivo Selection and Proteomic Analysis

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Supporting Information

ABSTRACT: Leishmaniasis is a neglected tropical disease caused by *Leishmania* protozoa. Two main forms are found in the Old World, self-limited cutaneous leishmaniasis and potentially fatal visceral leishmaniasis, with parasite dissemination to liver, bone marrow, and spleen. The *Leishmania donovani* species complex is the causative agent of visceral leishmaniasis worldwide, but atypical *L. donovani* strains can cause cutaneous leishmaniasis. We hypothesized that *L. donovani* can adapt to survive in response to restrictions imposed by the host environment. To assess this, we performed in vivo selection in BALB/c mice with a cutaneous *L. donovani* clinical isolate to select for parasites with increased capacity to survive in visceral organs. We then performed whole cell proteomic analysis and compared this visceral-selected strain to the original cutaneous clinical isolate and to a visceral leishmaniasis clinical isolate. Overall, there were no major shifts in proteomic profiles; however, translation, biosynthetic processes, antioxidant protection, and signaling were elevated in visceral strains. Conversely, transport and trafficking were elevated in the cutaneous strain. Overall, these results provide new insight into the adaptability of *Leishmania* parasites to the host environment and on the factors that mediate their ability to survive in different organs.

KEYWORDS: visceral leishmaniasis, proteomic analysis, virulence, pathogenesis

