THE CYTOSOLIC TRYPAREDOXIN IS ESSENTIAL FOR LEISHMANIA INFANTUM SURVIVAL

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Tryparedoxins are promising candidates for drug development. In *Leishmania infantum* the cytosolic tryparedoxin, *Li*TXN1, may be a key element in detoxification of reactive oxygen and nitrogen species. Moreover, *Li*TXN1 can potentially be involved in other cellular events such as DNA synthesis, which enhances its importance as a drug target. To validate this enzyme as an appropriate chemotherapeutic target its essentiality to the parasite had to be proven. Using a knockout strategy several attempts to replace both *Li*TXN1 alleles were unsuccessful and this could only be achieved upon previous complementation with an episomal copy of the gene. Maintenance of the episome in the absence of drug pressure proved gene essentiality both in promastigotes and in amastigotes recovered from mice. In attempt to understand the main role of this protein in the cell, single knockout mutants were assessed for their growth rate, hydrogen peroxide sensitivity and infectivity but no major differences were observed towards wild-type cells. Interestingly, determination of *Li*TXN1 amounts in single knockout promastigotes revealed that these parasites can modulate protein expression since they present around 75% of the enzyme, instead of the expected 50%. On the whole, the results in this presentation support the *Li*TXN1 crucial role to the parasite and reveal an interesting protein expression modulation which must be further investigated.