Comparative transcriptome profiling of virulent and non-virulent *Trypanosoma cruzi* underlines a role of surface proteins during infection

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Trypanosoma cruzi, the protozoan that causes Chagas disease, has a complex life cycle involving several morphologically and biochemically distinct stages that establish intricate interactions with various insect and mammalian hosts. It has also a heterogeneous population comprising strains that shows distinct properties such as virulence, sensitivity to drugs, antigenic profile and tissue tropism. We analyzed transcriptome data from two cloned *T. cruzi* strains that display contrasting virulence phenotypes in animal models of infection: CL Brener is a virulent strain and CL-14, a strain that is neither infective nor pathogenic in in vivo models of infection. RNA-seq analysis of CL Brener epimastigotes, trypomastigotes and intracellular amastigotes harvested at 60 and 96 hours post-infection (hpi) of human fibroblasts revealed large differences in their gene expression profiles. These changes reflect the parasite's adaptation to distinct environments during the infection of the insect vector and mammalian cells, including changes in energy sources, oxidative stress responses, cell cycle control and cell surface components. Whereas an extensive transcriptome remodeling was observed when CL Brener trypomastigotes were compared to 60 hpi amastigotes, only minor differences were observed between 96 hpi amastigotes and trypomastigotes of CL Brener. In contrast, the differentiation of the avirulent CL-14 from 96 hpi amastigotes to trypomastigotes was associated with considerable differences in gene expression particularly in genes encoding surface proteins such as trans-sialidases and the mucin associated surface proteins (MASPs). Thus, our comparative transcriptome analysis indicates that the avirulent phenotype of CL-14 may be due, at least in part, to a reduced or delayed expression of genes encoding surface proteins that are associated with the transition of amastigotes to trypomastigotes, an essential step in the establishment of the infection in the mammalian host.