

# Definition and comparative analysis of the kinomes of *Leishmania infantum* and *L. braziliensis*

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The parasites of genus *Leishmania* are causative agents of leishmaniasis, an endemic disease in 98 countries grouped as neglected tropical disease by the World Health Organization. There are only few drugs available for the treatment and they face issues such as toxicity, lack of efficacy, route of administration and emergence of resistant strains. Therefore, it is urgent to search for new drug targets in *Leishmania*. Protein kinases (PKs) are potential drug targets given their essential role in many biological processes. We performed a proteome-wide analysis of PKs of the species *L. infantum* and *L. braziliensis* using a refined bioinformatics pipeline. First, we classified the PKs from both species proteomes using Kinannotate software. Then, we added orthologous kinases from previously established kinomes of close organisms using the softwares OrthoMcl and OrthoVenn. We also curated our classification by constructing hidden Markov models (HMM) profiles of kinase groups from close organisms and searched through both species proteomes. Next, we performed a multiple alignment of the kinase domains and constructed a phylogenetic tree using the softwares MAFFT, Muscle and MEGA7. Then, the functional annotation of the predicted kinases was performed using Interproscan, KEGG and Gene Ontology terms. In order to find kinases that could be druggable targets, we searched for their essentiality at TriTrypDB and selected proteins associated with lethal phenotype. As a result, a total of 211 and 204 PKs were identified in *L. infantum* and *L. braziliensis*, respectively. The eukaryotic (ePKs) were classified into six of the nine major kinase groups and many kinases could be classified into family and subfamily levels. The most representative groups were CMGC (n= 50/48) and STE (n = 42/41). The poorly representative groups were AGC (n = 13/11), CAMK (n = 23/22) and CK1 (n = 7/7). The comparison of the kinomes of *L. infantum* x *L. braziliensis*, *L. infantum* x *L. major* and *L. infantum* x *Homo sapiens* showed a range of sequence identity between 77-81%, 81-94% and 33-47%, respectively. When we searched for essential kinases with lethal phenotype, 3 kinases were found: a polo-like PK (LinJ.17.0770), which is involved in signal transduction, cellular growth and apoptosis; an aurora kinase (LinJ.28.0550), involved in mitosis; and a casein kinase (LinJ.35.1030), involved in signal transduction. In conclusion, this bioinformatics pipeline provided the definition of *L. infantum* and *L. braziliensis* kinomes and could be useful for further studies of protein kinases as drug targets for antileishmanial drug design.