Bioinformatics approaches to identify, classify and prioritize protein kinases as drug targets in *Schistosoma japonicum*

Arthur de Carvalho e Silva[1], Joyce Villa Verde Bastos Borba[1], Pablo Ivan Pereira Ramos[2], Nicholas Furnham[3], Carolina Horta Andrade[1]

[1]Laboratory for Molecular Modeling and Drug Design, Faculty of Pharmacy, Federal University of Goiás, [2]Gonçalo Moniz Institute, Oswaldo Cruz Foundation (FIOCRUZ), [3]London School of Higiene and Tropical Medicine.

Schistosoma japonicum is one of the parasitic flatworms that causes schistosomiasis, a neglected tropical disease responsible for 200,000 deaths annually and affects more than 600 million people in Africa, Asia and South America. In this context, the main goal of this work was to determine the kinome complement within the *S. japonicum* proteome through bioinformatics tools, while also identifying essential kinases for the parasite that could serve as drug targets candidates. The proteome of *S. japonicum* was downloaded from GeneDB database. Next, the Kinannote tool was employed to generate a draft kinome, identifying 165 protein kinases candidates within the *S. japonicum* proteome. In a third step, kinases that Kinannote was not able to identify and classify were searched by means of orthology mapping with respect to *S. haematobium and S. mansoni*. The kinomes of both species were extensively used to analyze the orthology groups generated via OrthoMCL and OrthoVenn software, an approach that allowed the grouping of proteins from the three organisms. Using this strategy, the number of identified protein kinases in *S. japonicum* increased to 221. Functional annotation was made using KEGG and Gene Ontology terms, allowing the inference of subcellular localization and biological processes that each protein could be involved. MAFFT and MEGA7 software were used to build a phylogenetic kinome tree to help the visualization of the relationships between the kinase groups of *S. japonicum*. As a result of the classification, 7 kinases of *S. japonicum* were exclusively assigned to groups level, 103 kinases were assigned to groups and families; and 111 could be further classified into subfamilies. Kinases of *S. japonicum* were classified into nine major kinase groups: AGC (n=27), CAMK (n=35), CK1 (n=8), CMGC (n=38), Other (n=36), RGC (n=3), STE (n=22), TK (n=32), TKL (n=12) and atypical (n=8). STRING webserver was then utilized to generate a protein-protein interaction network based on *S. mansoni* data to study essentiality of some *S. japonicum* kinases. OrthoVenn analysis revealed 166 clusters of shared protein kinases among *S. japonicum*, *S. mansoni* and *S. haematobium* with a range of 75-85% of sequence identity and 116 clusters containing human orthologues shared by the three species. In conclusion, the present pipeline allowed the elucidation of the *S. japonicum* kinome and provides insights for next steps in the context of anti-schistosomal drug discovery.