EXPLORING EPIGENETIC TARGETS TO FIGHT NEGLECTED DISEASES: SELECTIVE SIRTUIN-2 INHIBITORS AS LEISHMANICIDAL COMPOUNDS

The disease burden of leishmaniases is widely studied and is an important instrument to plan a strategy to control or prevent this disease. One featured scenario is the lack of innovation in drug discovery toward novel anti-parasitic agents to control and treat leishmaniases. This is an important concern, and the genome sequencing of several Leishmania species is able to accelerate the identification of new drug targets. In this context, the parasites epigenome rises as an interesting target to drug discovery programs. Epigenetics comprises a series of chemical modifications of DNA and their associated histone proteins and it is known to be an especially important aspect of parasite biology, although it is underexplored in drug discovery programs. In this context, this project targets at the parasitic Sirtuins, which are important epigenetic regulator enzymes that acts in the deacetylation of the N-terminal tails of histones. This family of proteins is known to be essential for parasitic growth and the recent identification of sirtuin-related gene from L. amazonensis opened the possibility for the development of novel and specific sirtuin-based drugs. Our proposal is to develop a library of inhibitors for L. amazonensis sirtuin-2 based on a computer-aided drug discovery and classical medicinal chemistry approaches. The proposal is multidisciplinary and brings together molecular parasitology, enzymology, medicinal chemistry, organic synthesis and pharmacology toward the development of a versatile platform to explore the epigenetic of L. amazonensis to find drug candidates to treat leishmaniasis and also diseases caused by other trypanosomatides.

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ABOUT THE PROJECT

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