Antimony resistance in *Leishmania donovani*: a metabolomics study on the promastigote life stage

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Thanks to significant improvements in LC-MS technology, metabolomics is increasingly used as a tool to discriminate the responses of organisms to various stimuli or drugs [1]. In this study, we implemented an untargeted LC-MS metabolomics approach to gain insights in metabolic differences between clinical antimonial-(SSG)-sensitive and SSG–resistant *Leishmania donovani* isolates in the promastigote life stage.

In a first stage, we compared the metabolic profile of three strains with a different antimony susceptibility profile in two different growth stages of the promastigote life stage: the logarithmic growth stage and the stationary growth stage. This showed that the majority of metabolic changes related to SSG-resistance occurs only in the stationary growth stage, which is in accordance with the hypothesis that during this life stage the parasite will prepare to encounter the host where it can be exposed to the drug. Interestingly, we disclosed several complete metabolic pathways which are upregulated in two SSG-resistant strains such as the cysteine pathway and the ureum cycle, both contributing to the production of thiol-containing metabolites which are involved in protection against oxidative stress. Increased levels of amino acids and purine nucleosides were detected as well, which might be related to the higher fitness of SSG-R parasites by providing a 'survival kit' during the initial stage of host infection [2].

In a second stage we also studied the metabolic effect of Sb^{III} drug pressure on one of these SSG-resistant lines. Exposure to this drug further affected the thiol levels, showing how this resistant parasite deals with the encountered oxidative stress imposed by Sb^{III}.

References

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