Characterization of Schistosome Lysine Specific Demethylase 1 (LSD1) as a potential drug target

MONTEIRO, P. H S.[1], CARNEIRO, V.C[1], TORRES, E. J. L. [2] , , AMARAL, M. S.[3], ANDRADE, A. [3],VERJOVSKI-ALMEIDA, S.[3], , BORRELLO, T.[4],GANESAN, A.[4], ROTILI, D[5], MAI , A[5], DE ABREU DA SILVA, I. C[1], LANCELOT, J.[6], PIERCE, R.J.[6], FANTAPPIÉ, M. R[1]

[1] Instituto de Bioquímica Médica, Programa de Biologia Molecular e Biotecnologia, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brasil, [2] Universidade do Estado do Rio de Janeiro, Faculdade de Ciências Médicas, Rio de Janeiro, Brasil, [3] Instituto de Química, Universidade de São Paulo, São Paulo, Brazil,[4] University of East Anglia, Norwich Research Park, UK, [5] Department of Drug Chemistry and Technologies, Sapienza University of Rome, Italy [6] CIIL, INSERM U1019 – CNRS UMR 8204, Université Lille Nord de France, Institut Pasteur de Lille, France.

Introduction: Schistosomiasis is a chronic disease that affects 240 million people in the world with still only one efficient drug, Praziquantel. The development of new drugs is therefore mandatory. The new strategy that we have chosen is to target the enzymes involved in epigenetic modifications of the chromatin, such as methylation of histones. In the present work, we show that specific inhibition of the histone demethylase LSD1 from *S. mansoni* affects worm pairing and egg laying.
Objective: Test synthetic LSD1 inhibitors as a new strategy to control Schistosomiasis.
Methodology: Drug screening of *S. mansoni*, by in vitro culture of adult worms; Viability estimation and quantification by ATP measurements; Confocal Laser Scanning Microscopy of the adult worms and quantitative RT-PCR. Western Blot analysis of the methylation status of the Histone H3. Transcriptomic analysis (RNAseq) of treated juvenile and adult schistosomes.
Results: We have identified a potent compound showing high toxicity leading to complete mortality of adult worms after 72h at a dosage of 10-25 uM. Egg laying by adult female schistosomes was significantly affected by the LSD1 inhibitors. The LSD1 compounds showed specificity, as measured by the increase of H3K4(2met) levels in the treated parasites. Importantly, several genes were differentially expressed in adult schistosomes upon LSD1 inhibition.
Conclusions: So far, we have validated LSD1 inhibitors as a novel and promising strategy to control schistosomiasis.
Key Words: Epigenetics, *Schistosoma mansoni* and Lysine demethylation, Chromatin, Therapeutics.
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