Metabolomics for global characterisation of phenotypic diversity in *Leishmania* populations

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Leishmania phenotyping was until recently mostly limited to what can be observed in a controlled *in vitro* or *in vivo* environment e.g. survival upon drug exposure. However, the arrival of metabolomics is drastically changing the concept of phenotyping. The metabolome (the set of metabolites present in a biological system) lies downstream of the transcriptome, proteome and any post-translational events, and can be regarded as the ultimate expression of an organism's genotype, the closest correlate to the phenotype. In this study we carried out metabolome-wide comparison of multiple antimonials-sensitive and -resistant *L. donovani* isolates using ultra high resolution Fourier Transform mass spectrometry, a technology that allows rapid, accurate and precise whole metabolome profiling. The results of this study demonstrate how revealing the diversity on whole metabolome level in a natural *Leishmania* population can significantly contribute to (i) distinguishing the different phenotypes present in a population, (ii) giving a global overview of all factors involved in drug resistance by highlighting entire metabolic pathways, and (iii) enhancing our understanding of parasite flexibility. The used methodology, from sample preparation to identification of metabolic signatures of drug-resistant parasites, will be presented and discussed in the context of future applications for *Leishmania* research.

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