

## ***Leishmania* as a paradigm for exploring the impact of genome diversity on metabolome variation**

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The genome and the metabolome are situated at the extreme ends of the modern dogma of molecular biology. The natural diversity of microorganisms provides the context for innovative studies on the functional link between these two '-omes'. We use a Nepalese population of *Leishmania donovani* characterised by a high phenotypic diversity (antimonial drug susceptibility, infectivity...). Full-genome sequencing of 17 *L. donovani* lines revealed a low diversity at the sequence level, but a high diversity at the structural level (aneuploidy, tandemly repeated genes, episomes). We hypothesise that this structural variation drives the evolutionary flexibility and adaptive capacity of *L. donovani*. We are currently investigating how the observed diversity on genome level is manifested on the level of metabolic diversity. A proof-of-principle metabolomics study already demonstrated that 1/3 of all detected metabolites were showing significantly different levels between antimony-resistant and sensitive strains. A similar global metabolomic characterisation is currently in progress for all clinical lines which were studied on genome level. The resulting metabolome diversity data will be related to the genomic diversity data for all 17 clinical lines. We anticipate that this integrative approach will give an unprecedented insight into pathogen diversity.