Whole comparative genome sequencing reveals several levels of genomic diversity among *Leishmania donovani* strains in Indian subcontinent.

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Leishmania donovani (*L. donovani*) of the Indian subcontinent causes visceral leishmaniasis, a disease characterized by extensive variability in clinical manifestation. This contrasts with the low genomic heterogeneity found so far in this parasite population. New sequencing technologies now offer the possibility to characterize the whole genome of multiple strains and better assess its impact on phenotypic diversity. In the frame of the GeMInI project (the Genome and Metabolome Integrated Initiative, www.leishrisk.net/gemini), we apply this concept to *L. donovani*, using drug resistance as a paradigm of phenotypic diversity.
After construction of a *de novo* reference sequence of *L. donovani*, genomic diversity was assessed among strains derived from 20 Nepalese clinical isolates. Three types of genomic diversity elements were identified: (i) single nucleotide polymorphisms (SNPs), (ii) copy number variations (CNVs) and (iii) whole chromosome duplications. Coding SNPs were correlated with observed clinical phenotypes and previously observed population structure. Several large scale CNVs were also identified. The most unexpected genomic diversity was found at the level of chromosome number and ploidy which appeared to be strain-specific. We are currently examining the functional impact of these findings and in the near future plan to integrate genomic diversity results with metabolomic diversity elements identified in parallel in our GeMInI study.