

Patterns of population genomic variation in *Leishmania donovani*.

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The development of high-throughput sequencing platforms enables a deeper and more comprehensive exploration of genomic variability in disease-causing parasites. Using 454 and Illumina sequencing technologies, the Gemini and Kaladrug consortia have resequenced over 20 *Leishmania donovani* field isolate genomes obtained from Kala-Azar patients showing different responses to antimonial treatment and different in vitro susceptibility to antimonies. Fourteen of these strains were examined further here. These high-quality genome sequences cover over 95% of chromosomal sites based on a reference sequence constructed from the *L. infantum* genome, yielding 6,280 candidate SNP sites. 748 of these were located in coding regions and 463 of these cause changes at the protein sequence level. About one third (1, 854) of the candidate SNP sites were uniformly heterozygous, indicating that nucleotide variation may be preserved at key regions: 210 of these SNPs were in protein-coding sequences. The restricted number of amino acid-changing sites (21) with high (> 0.4) folded allele frequencies that were not uniformly heterozygous in the 14 *L. donovani* samples indicates that a limited number of key changes may be related to the variable phenotypes of these strains in humans. Further analysis may refine and elucidate the relationship between genetic variation in *L. donovani*, treatment outcome and in vitro drug susceptibility.