

# The genome of *Leishmania donovani* from clinically isolated parasites in India and Nepal: structural variations

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## Introduction

- We are conducting a comprehensible analysis of genomic diversity in *L. donovani* of the Indian sub-continent and exploring its relevance to clinical polymorphism and epidemiological dynamics.
- New sequencing technologies and assembly tools developed at the Sanger Institute generated a high quality draft of the *L. donovani* genome sequence (combination of 454 and Illumina). The high-coverage genome sequences of 17 clinical Nepalese and Indian strains sensitive or resistant to antimonials were mapped to the reference.



## 1. Copy number variation (CNV)

### • Inter chromosomal CNV (Ploidy variation)

- whole scale deletion and duplication of a chromosome



### • Intra chromosomal CNV

- partial scale deletion and duplication of a chromosome

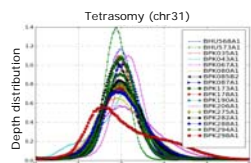
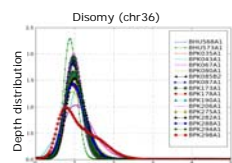
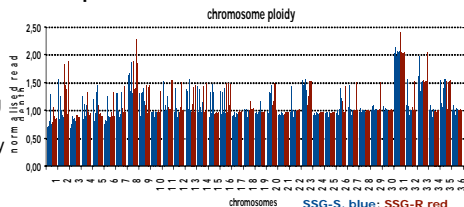


## 2. Ploidy diversity

### Distribution of sequencing read-depth

for the 36 chromosomes in a sample of 13 *L. donovani* strains.

- ploidy is chromosome-specific, with some showing stable disomy, stable tetrasomy or variable ploidy
- whole chromosome variation is strain-specific



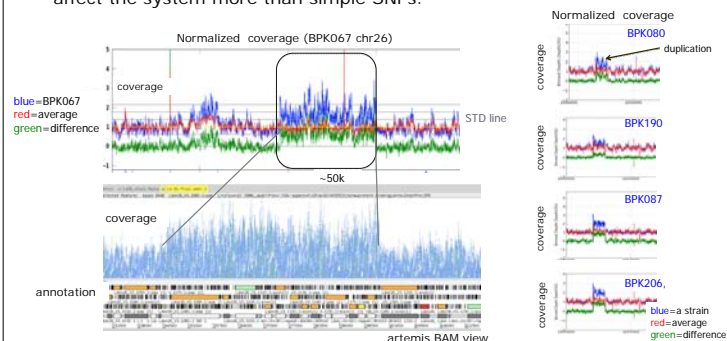
## 3. Duplication

### • Shared Duplication

Shared among a group.

### • Duplication

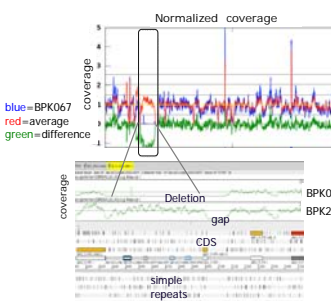
Many genes duplicated in this region can affect the system more than simple SNPs.



## 4. Deletion

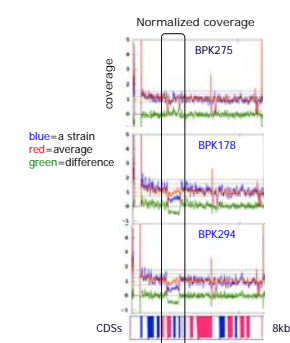
### Single complete deletion

- deleting a gene



### Single shared partial deletion

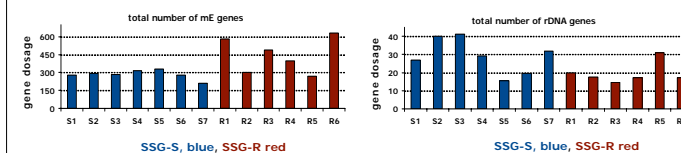
- affecting a few genes



## 5. Gene dosage (ploidy & CNV)

Quantitative analysis is another application of sequencing read-depth: copy number of mini-exon (mE) and rDNA genes per haploid genome (test case)

- values fit very well with published ones (83-170 mE, 7-18 rDNA)
- expansion-contraction of the tandem arrays is common
- in combination with ploidy changes, it generates gene dosage (figure)
- functional importance to be explored: the 4 strains showing a higher total number of mE genes are all SSG-resistant



## 6. Conclusions and prospects

- Ploidy** is the most prevalent genomic diversity among *L. donovani* strains. Its biological significance and implication are now being investigated to understand the reasons behind this high ploidy diversity.
- Gene dosage effects** like ploidy and CNVs may play a key role to gene regulations because it does not have some gene regulatory mechanisms that are common to other eukaryotic organisms.
- Metabolomics**: the same strains are being analysed at the metabolome level: integration of both datasets will enhance **systems biology** approaches in *Leishmania* research.
- Work in progress: we are developing new and simple software and tools for epidemiological monitoring of *Leishmania* for public.

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