



A novel genomic platform for parasite drug resistance diagnostics in *Leishmania infantum* through copy number variation analysis



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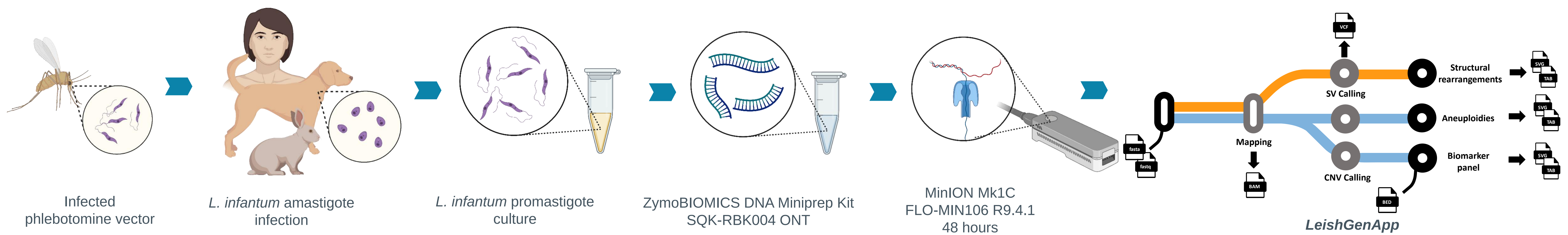


Introduction

- Leishmania infantum* is a protist parasite and causative agent of leishmaniasis, endemic to many countries world-wide, per example the Mediterranean basin.
- Emerging drug-resistant *L. infantum* is one of the most relevant neglected tropical disease, as it is responsible for 12M infections w/w and more than 25,000 deaths.
- It possesses a genome of 32 Mb distributed in 36 chromosomes and a complex network of maxi- and minicircle kinetoplasts (functionally similar to mitochondria).
- Its genome is structurally complex, with frequent rearrangements and aneuploidies. Such changes in copy number variation (CNV) occur as a result of environment adaptation and can be potentially used as genetic biomarkers to create a genetic resistance profile.

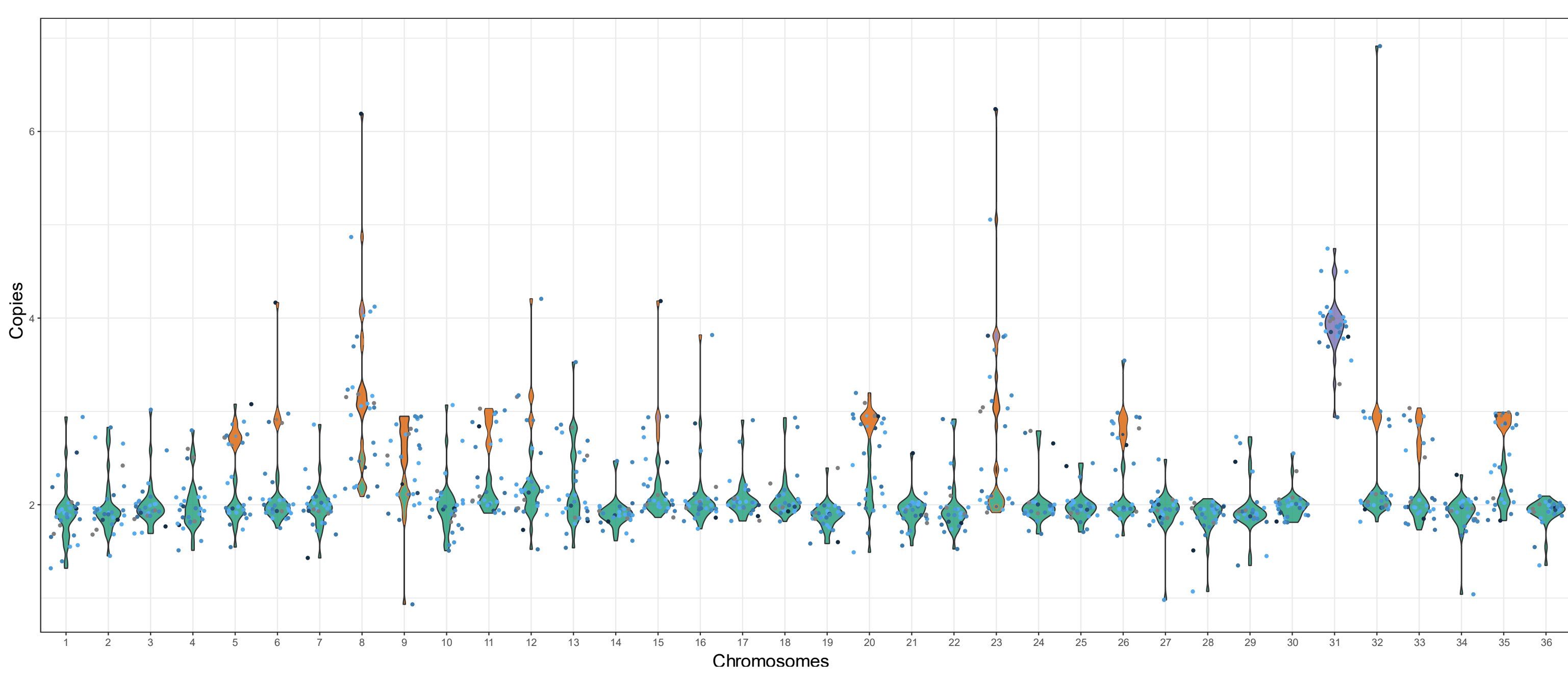


Material and Methods



Results

1. *L. infantum* aneuploidies and genome dotation



- Sequencing of 28 Mediterranean *L. infantum* isolates shows a wide variability in chromosome dotation
- Most chromosomes are present as 2N, except for chromosomes 31 (4N)
- L. infantum* displays alterations of chromosome dotation as continuum (mosaicism) or as discrete values (subpopulations)
- Chromosome variation is independent with culturing method, passage history, parasite host or country of isolation

- Each sample displays a different and specific CNV signature for its pharmacoresistance profiling (17 genes)
- Resistance is diverse and locally adaptative (no common origin)
- Multidrug resistance is frequent, and resistance to > 1 compound is the most common scenario
- High prevalence of resistance to commonly administrated drugs (allopurinol and antimonials)

2. *L. infantum* drug resistance CNV biomarkers

