Extensive structural variation in the genome of *Leishmania infantum*

Analyzing from small duplications to aneuploidies in the cloud

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The excellence in One Health genomics

Introduction

- *Leishmania infantum* (LI) is a protist parasite and causative agent of leishmaniasis, endemic to many countries world-wide (Figure 1).
- Currently, emerging drug-resistant *LI* is one o f the most relevant neglected tropical disease, as it is responsible for 12M infections w/w and more than 25,000 deaths.

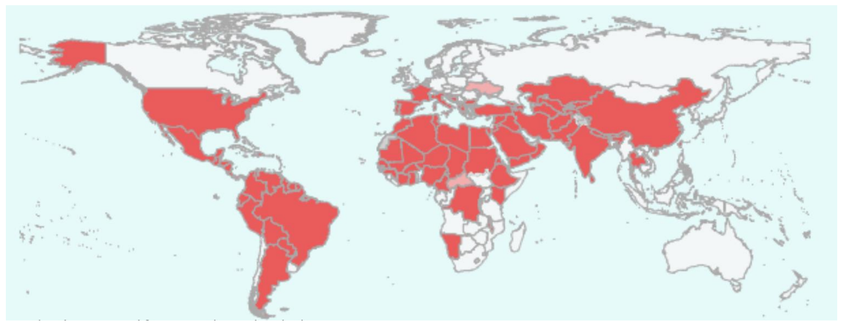

Figure 1. Leismaniasis endemic countries as per WHO

- *LI* genome has 36 chromosomes (32 Mb), complex and unstable with extensive structural variations (Figure 2).
- *Leishmania spp*. regulate their protein expression by genome and gene copy expansion.
- Copy number variation (CNV) can be used as biomarkers for virulence and resistance.

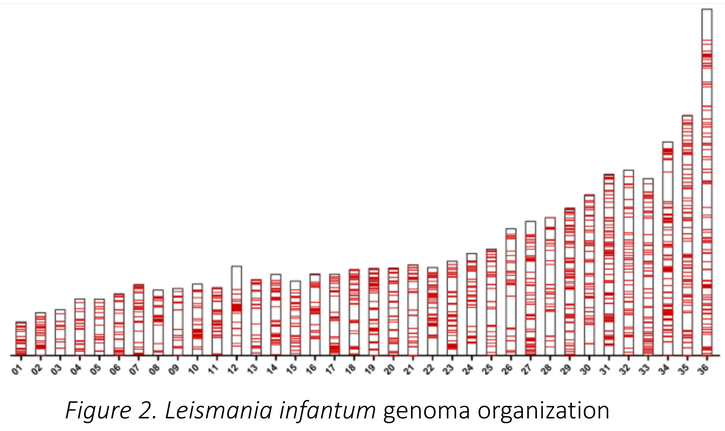

Figure 2. Leismania infantum genoma organization

Material & Methods

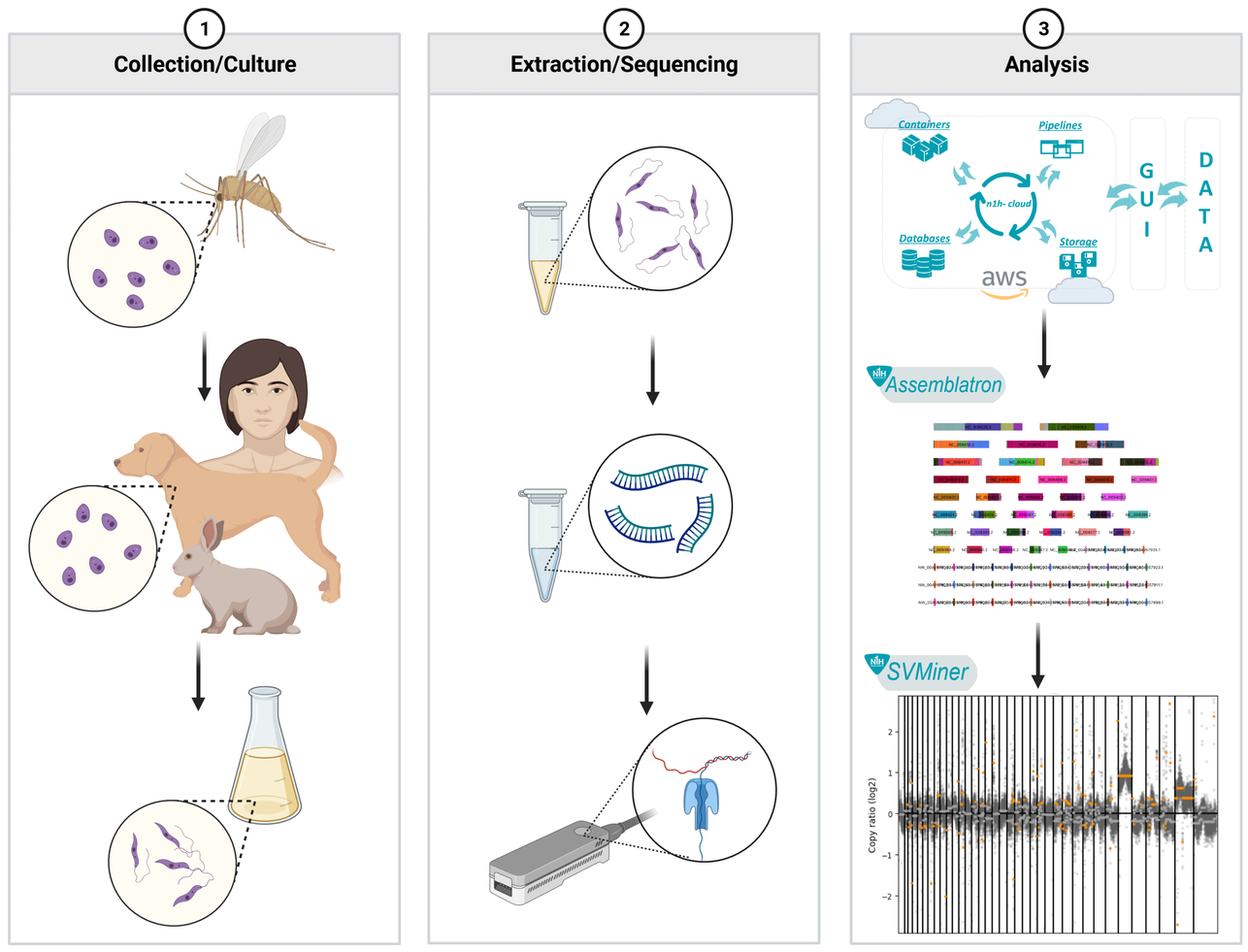

Figure 3. Graphic summary for Leishmania infantum

- Collected *LI* isolates from humans, dogs and rabbits are cultured in Schneider medium + 20% FBS + 2% urine.
- Amastigotes are collected at 1e6/ml and extracted using HMW Zymo MagBead kit (large fragments).
- DNA is sequenced natively using the RAD004 kit on a R9.4.1 flowcell.
- Data analysis is conducted through our up coming service *n1h-cloud* (custom pipelines).
  - *De novo* assembly.
  - SV discovery and CNV scanning.

Results

- As a proof-of-concept, a *LI* strain (derived from a case of cutaneous leishmaniasis) was sequenced through nanopore sequencing.
- Long-read sequencing revealed pervasive structural rearrangements (SV) in all *LI* chromosomes, consistent with genome instability during replication (Figure 4).
- Deletions and insertions were the most common SVs, consistent with changes in CNVs.

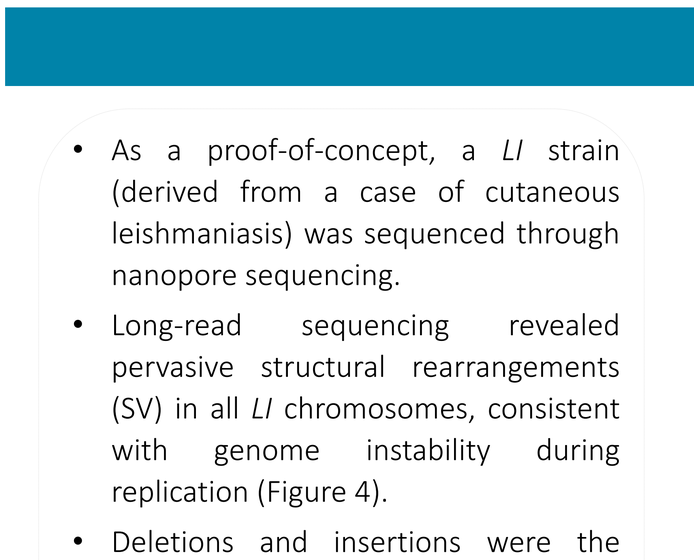

Figure 4. Structural rearrangement summary

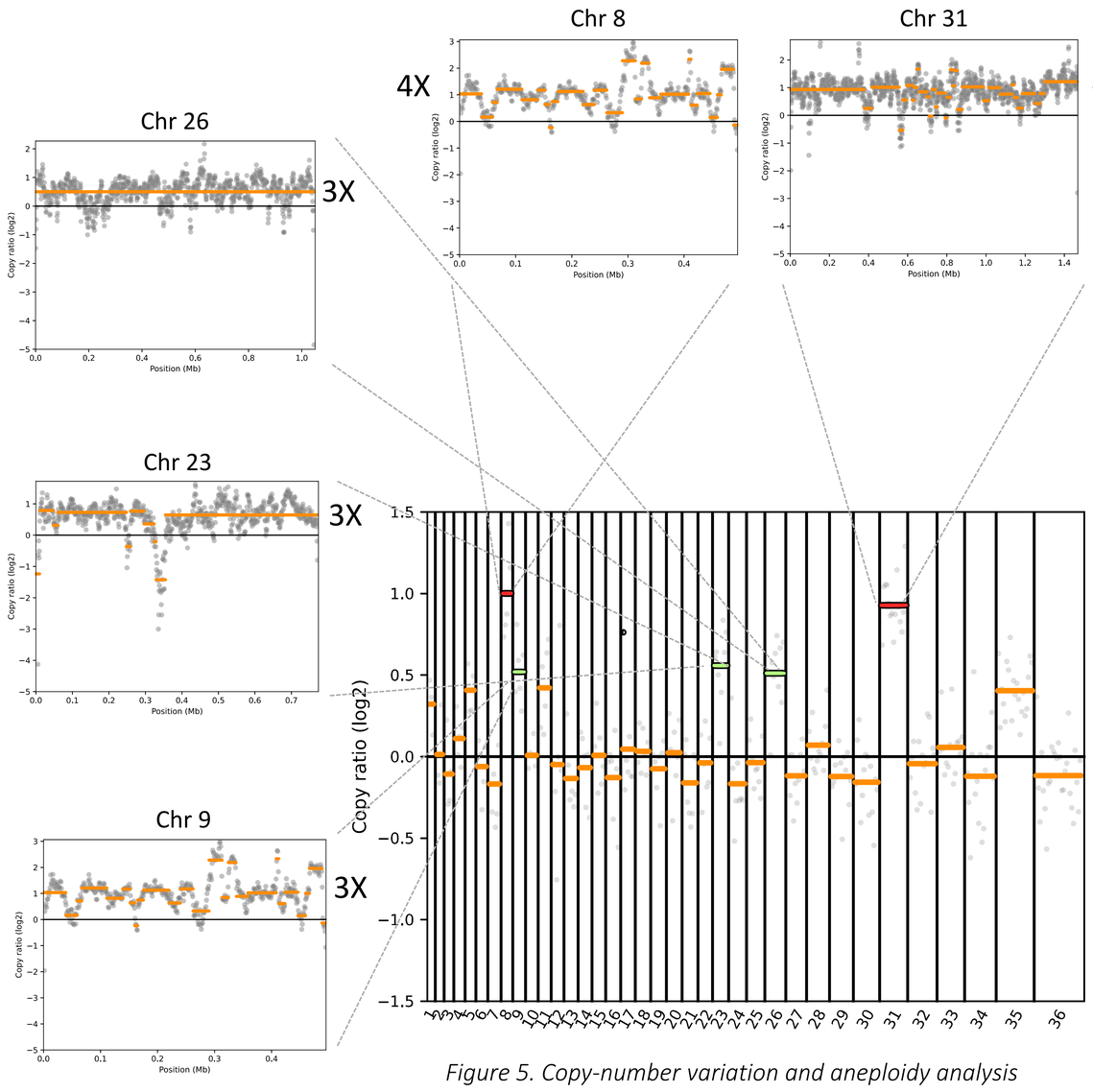

Figure 5. Copy-number variation and aneploidy analysis

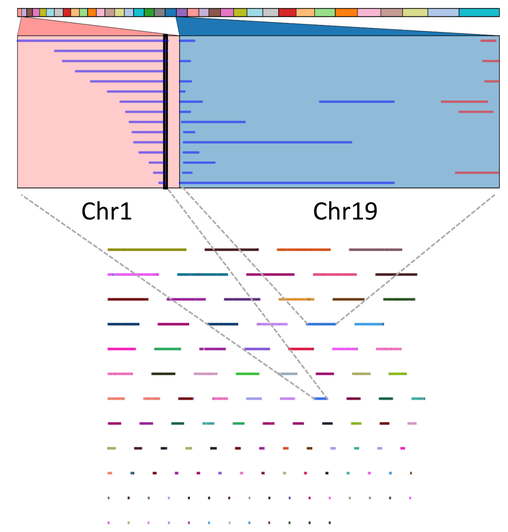

Figure 6. Interchromosomal rearrangements (chr1:chr19)

- CNV analysis detected complete (tetrasomy chr31) and partial (trisomy chr23) aneuploidies (Figure 5).
- CNVs can modify effective ploidy by local expansion and contraction (Figure 5).
- Interchromosomal rearrangements are less abundant but may play an important role of loss-of-function (chr1:ch19, Figure 6).

Conclusions

- Long-read sequencing was evaluated to detect SV in *Leishmania infantum*, an emerging drug-resistant thread world-wide.
- Genome rearrangements and CNV analysis through our up-coming data analysis service *n1h-cloud* revealed pervasive genome rearrangements, characterized by local CNV, in tandem with total or partial aneuploidy (putative biomarkers).
- Interchromosomal translocation was detected in several chromosomes, revealing added potential for genome shuffling and possible loss-of-function.

Acknowledgements

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SVGM

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