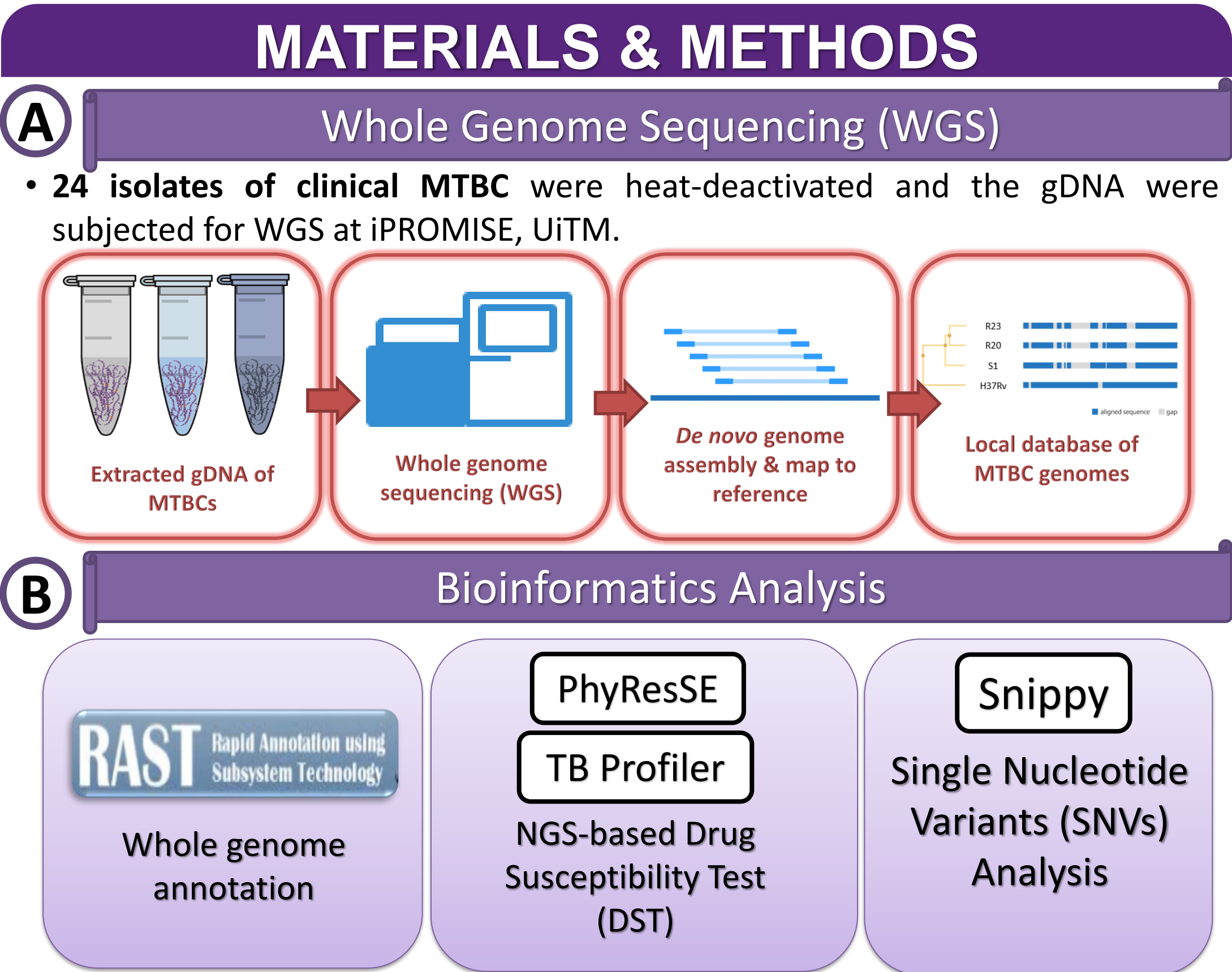


INTRODUCTION

- Tuberculosis is still a major health problem in Malaysia with thousands of cases reported yearly along with the emergence of multi-drug resistance tuberculosis (MDR-TB)¹.
- Identification and prediction of MDR-TB are important to ensure efficient TB management².
- Online annotation tools to analyse *Mycobacterium tuberculosis* complex (MTBC) genomes had been published for public use.
- Having local MTBC genome database allows identification of drug resistant variants which could be used to design diagnostic kits for detection of drug-resistant MTB.
- The current study is an initial effort in establishing MTBC genome database in Malaysia and demonstrates the application of the database in discovering the genetic diversity of the clinical MTBC isolates.



RESULTS & DISCUSSION

Genome Sequencing, Annotation & Phylogenetic Analysis

- A database of 24 MTBC draft genomes was established (average of **97%** completion and **107X** depth of coverage).
- Twenty seven single nucleotide variants (SNVs) with high confidence mutations were identified in genes associated with isoniazid (*fabG1*, *inhA*, *katG* and *kasA*), rifampicin (*rpoB*), ethambutol (*embB*), streptomycin (*rpsL* and *rrs*), pyrazinamide (*pncA*) and fluoroquinolones (*gyrA*) resistant isolates.

Table 1: Overall variant profile of the 24 MTBC draft genome.

Strains	Total variants	Non-synonymous variants	No. of genes involved
All	7,576	4,294	1,390 genes + 3,715 unannotated sites
Drug-resistant	5,739	3,259	1,231 genes + 2,794 unannotated sites
Drug-sensitive	4,889	2,751	1,132 genes + 2,446 unannotated sites

Note: Total identified genes in *M. tuberculosis* H37Rv: 4,124 genes.

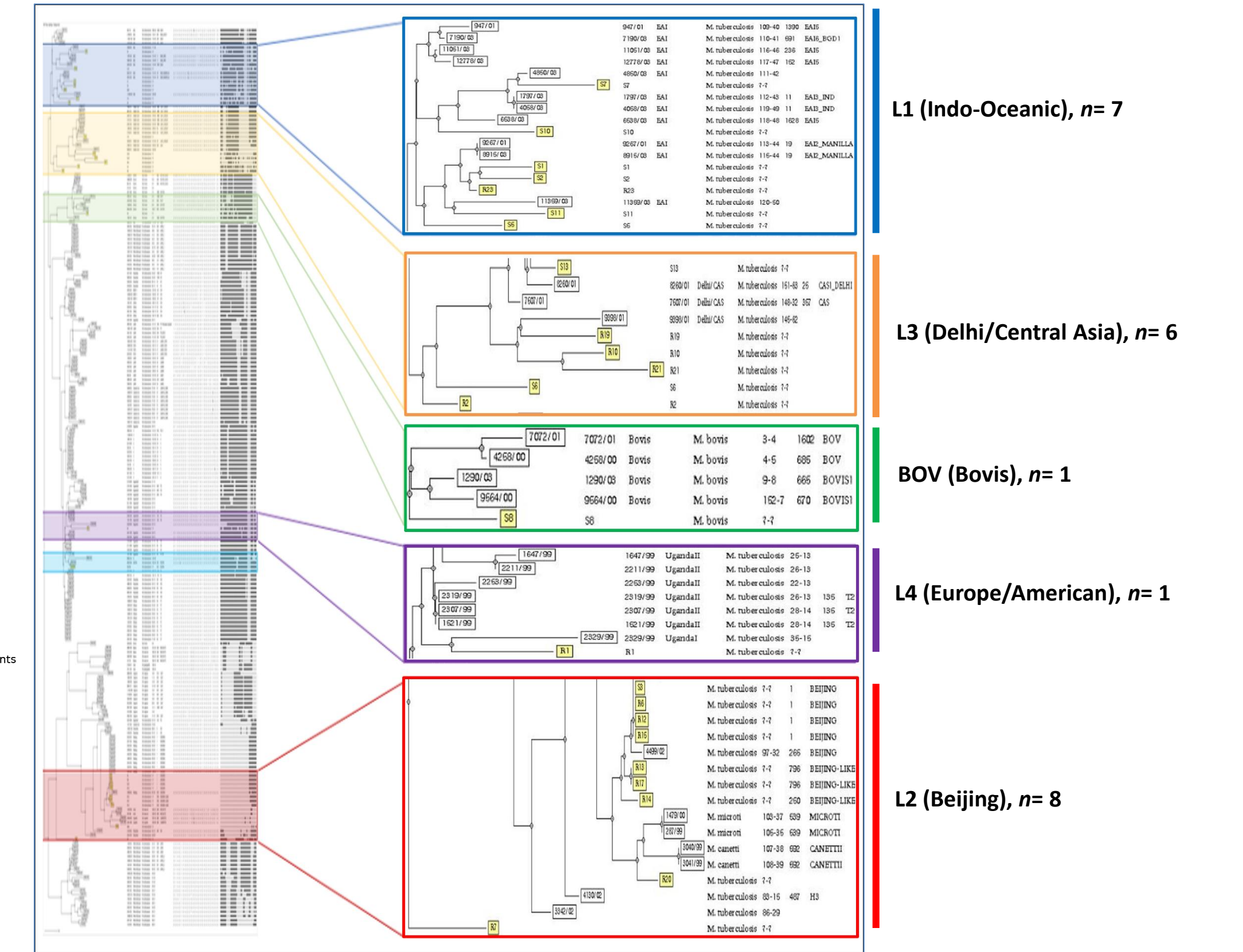
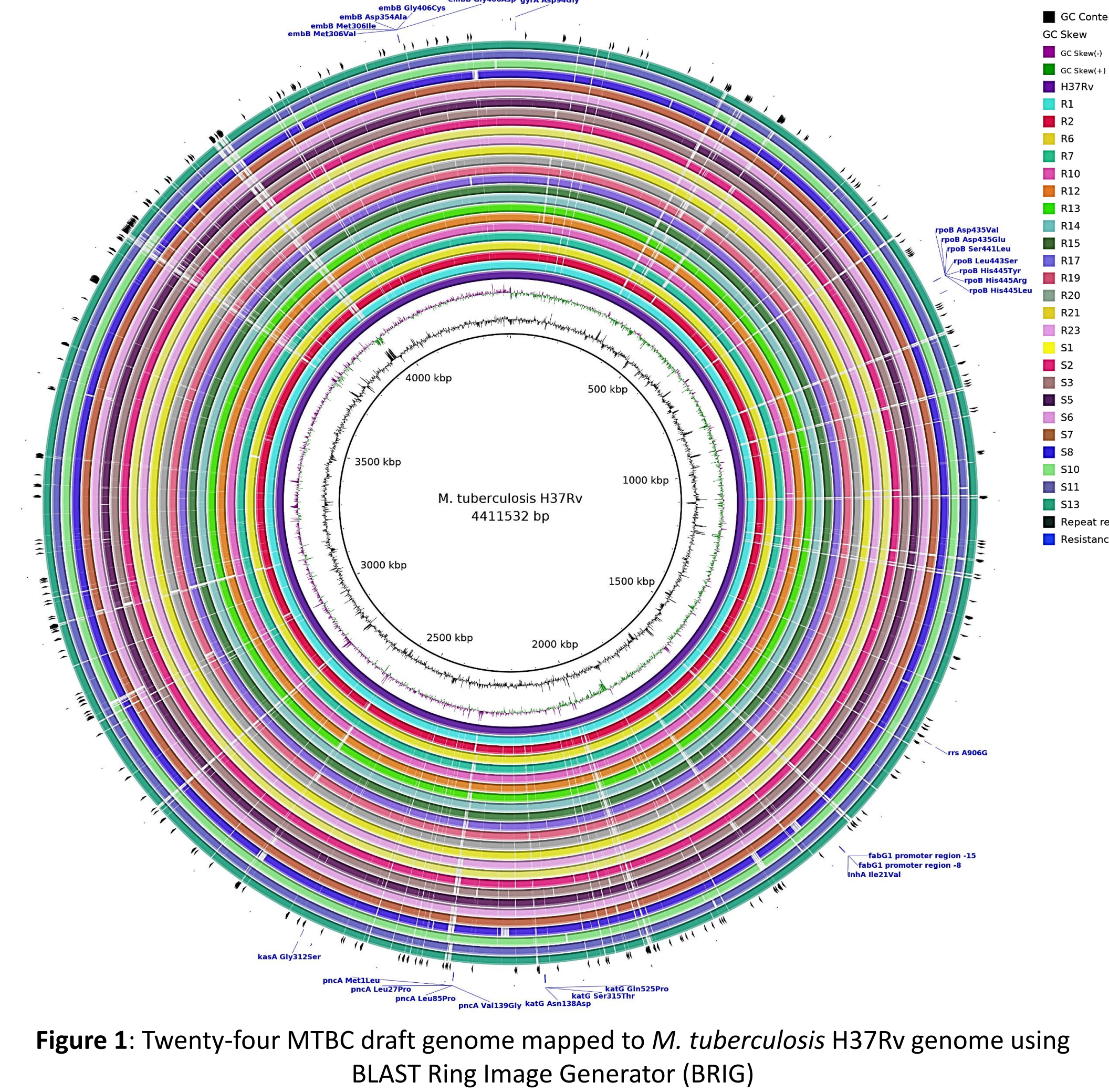


Figure 2: Phylogenetic tree based on NGS-based spoligotyping of the 24 MTBC isolates.

CONCLUSION

- Four lineages of *M. tuberculosis* were identified where majority of the isolates are L1 (Indo-Oceanic) and L2 (Beijing).
- A database of 24 MTBC genomes was established.