





Genomic-informed Initiative on Surveillance of MDR-TB in Malaysia



Institut Farmakogenomiks Integratif

Variants (SNVs)

Analysis

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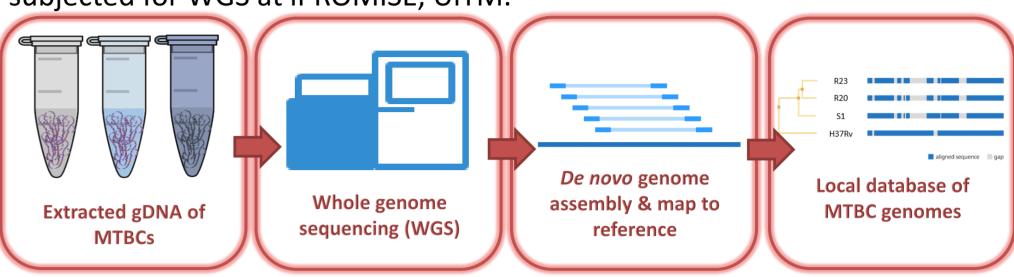
INTRODUCTION

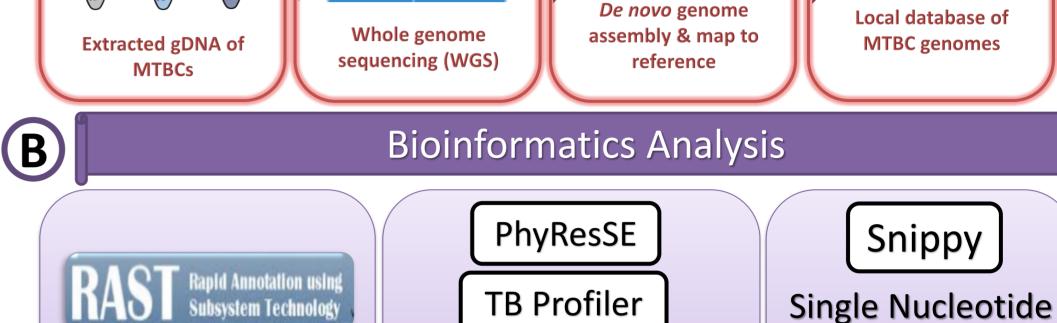
- Tuberculosis is still a major health problem in Malaysia with thousands of cases reported yearly along with the emergence of multi-drug resistance tuberculosis (MDR-TB)¹.
- Identification and prediction of MDR-TB are important to ensure efficient TB management².
- Online annotation tools to analyse 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.

MATERIALS & METHODS

Whole Genome Sequencing (WGS)

• 24 isolates of clinical MTBC were heat-deactivated and the gDNA were subjected for WGS at iPROMISE, UiTM.





NGS-based Drug

Susceptibility Test

(DST)

Genome Sequencing, Annotation & Phylogenetic Analysis

RESULTS & DISCUSSION

- 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.



Whole genome

annotation

table 1. Overall variant profile of the 24 wirds 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.

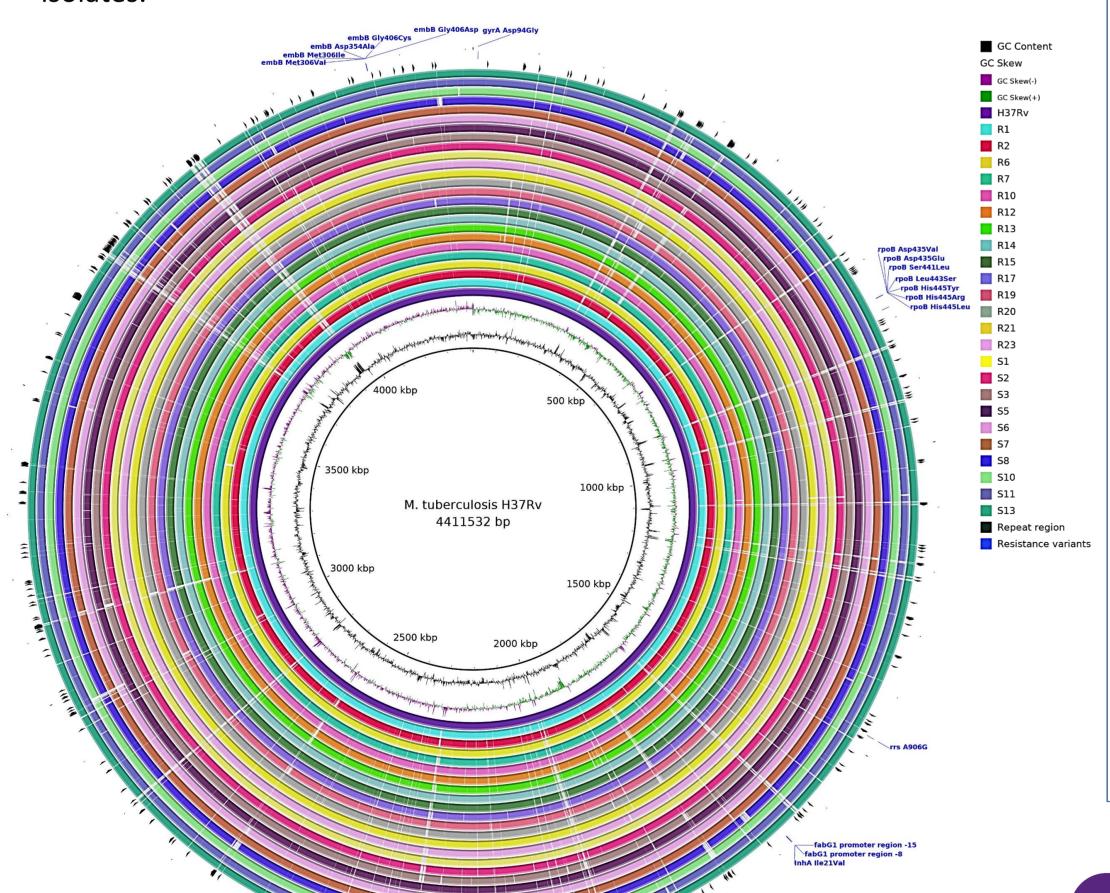


Figure 1: Twenty-four MTBC draft genome mapped to M. tuberculosis H37Rv genome using **BLAST Ring Image Generator (BRIG)**

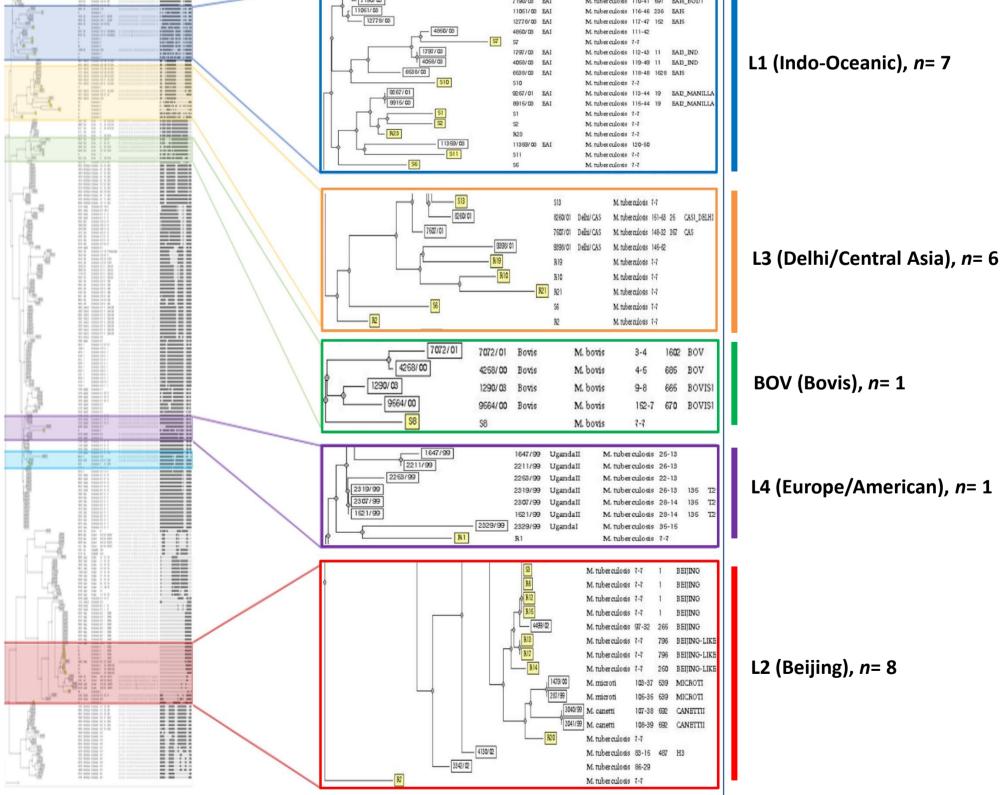


Figure 2: Phylogenetic tree based on NGS-based spoligotyping of the 24 MTBC isolates.

- ✓ Four lineages of *M. tuberculosis* were identified where majority of the
- A database of 24 MTBC genomes was established.

CONCLUSION

isolates are L1 (Indo-Oceanic) and L2 (Beijing).

1) World Health Organization. WHO Global Report, Global Tuberculosis Report 2010-2018. Geneva: World Health Organization; 2010-2018 2) Dheda et al., 2017. The epidemiology, pathogenesis, transmission, diagnosis, and management of multidrug-resistant, extensively drug-resistant, and incurable tuberculosis. The Lancet Respiratory Medicine, 5(4), 291-360.

Acknowledgements

References

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