Accelerating progress to end TB

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Bioinformatics identification of antituberculosis resistance and associated lineages using whole-genome sequence data.

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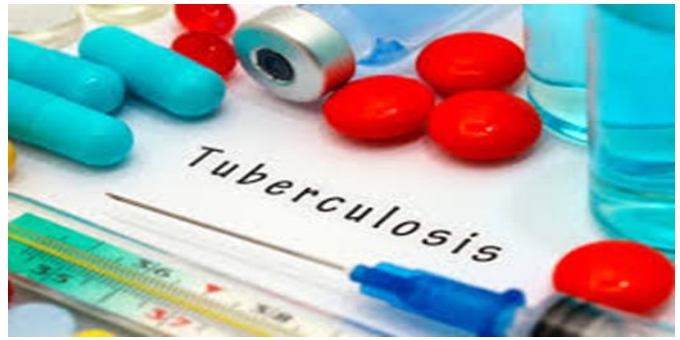


The South African Medical Research Council
recognizes the catastrophic and persisting consequences of colonialism and apartheid, including land dispossession and the intentional imposition of educational and health inequities.

Acknowledging the SAMRC's historical role and silence during apartheid,
we commit our capacities and resources to the continued promotion of justice and dignity in health research in South Africa.

INTRODUCTION

- Tuberculosis (TB) remains the deadliest Infectious disease worldwide
  - due to the increasing dissemination of multidrug and extensively drug-resistant (MDR/XDR) strain
- It is a significant contributor to the overall global disease burden, killing over a million people each year

Fist line drugs
Rifampicin (RIF)
Isoniazid (INH)
Ethambutol (EMB)
Pyrazinamide (PZA)

❑ **MDR**
RIF +INH

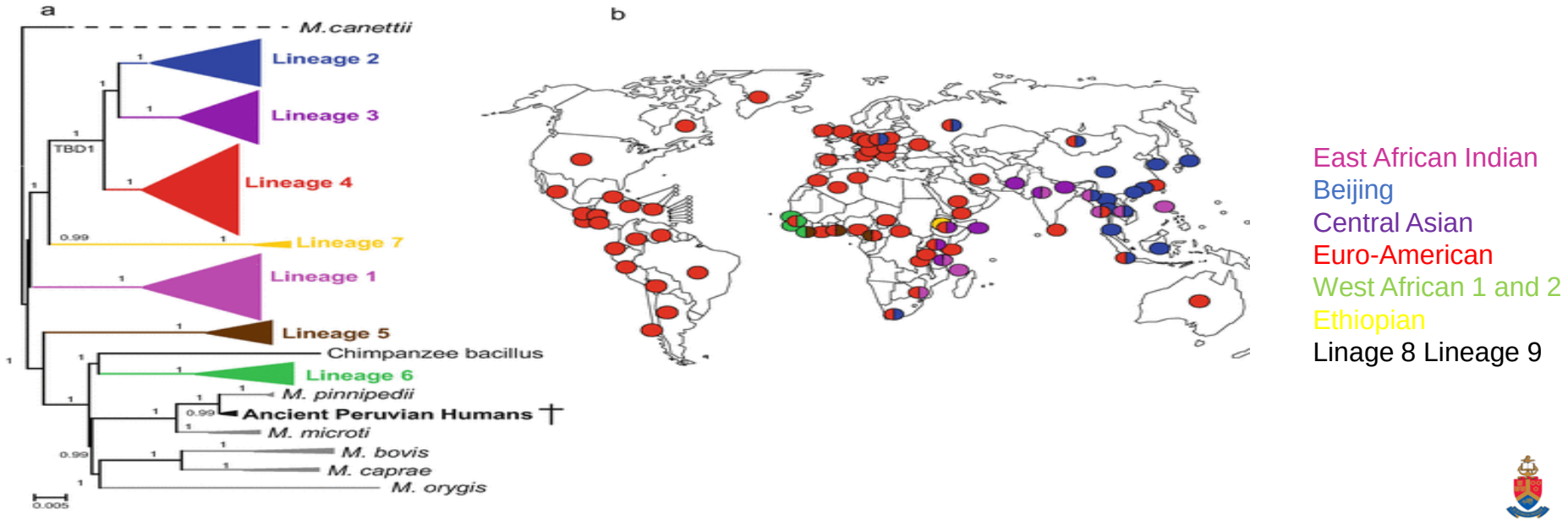
Second line oral drugs
Fluroquinolones (FQL):
Levofloxacin (LVX)
Moxifloxacin (MFX)
Bedaquiline (BDQ)
Clofazimine (CFZ)
Linezolid (LZD)

❑ **pre-XDR**
MDR +FQL

❑ **XDR**
MDR +FQL+ BQD/LZD

INTRODUCTION

- To eradicate TB, the transmission of drug-resistant *Mycobacterium tuberculosis* (MTB) strains must be reduced
- Thus, by understanding the drug-resistant determinant and lineages
- Nine lineages have been reported that represent a genetic diversity and global distribution of MTB strains



INTRODUCTION

- Whole genome sequencing (WGS) has been shown to have the potential to accelerate the detection of drug resistance surpassing the time taken by phenotypic drug susceptibility testing (DST) methods.
- This study determines the genotypic variants associated with MTB drug-resistance as well as its lineages through whole WGS and the culture-based drug susceptibility testing method

METHODS

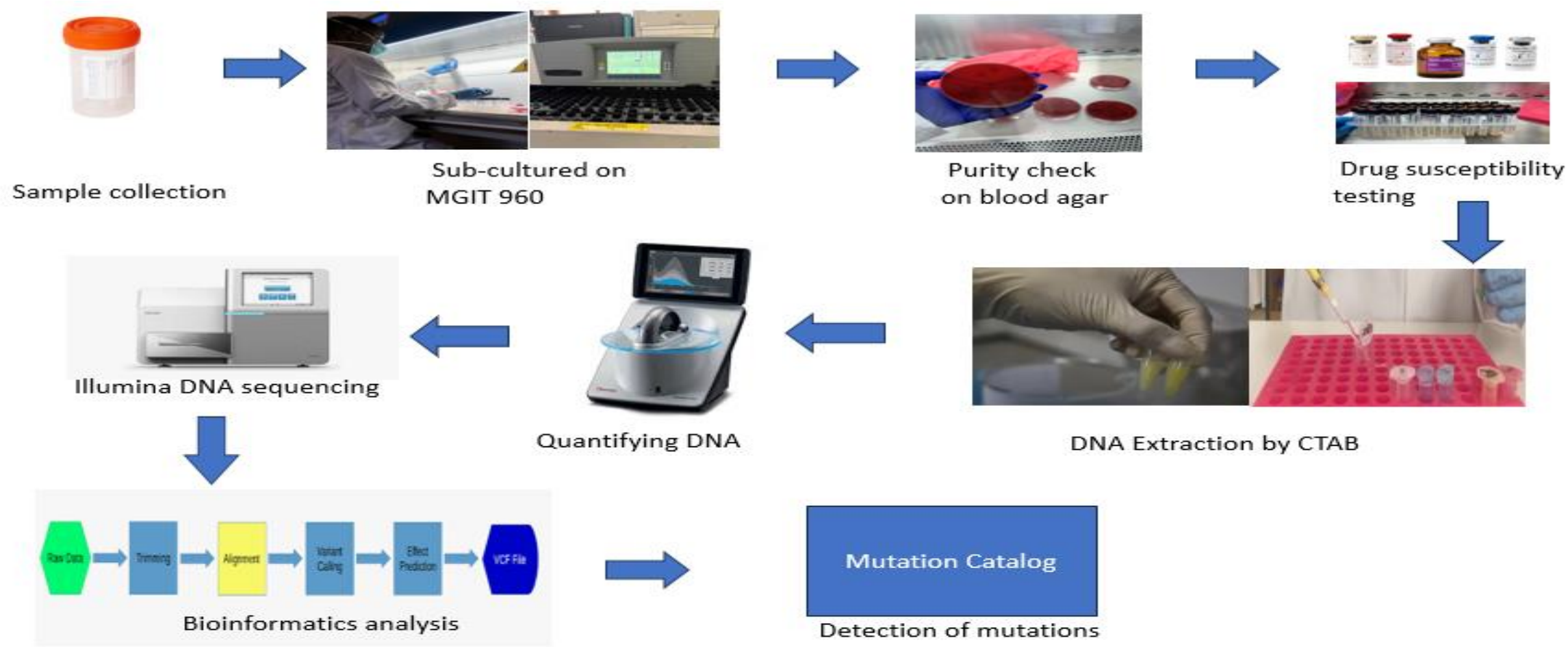
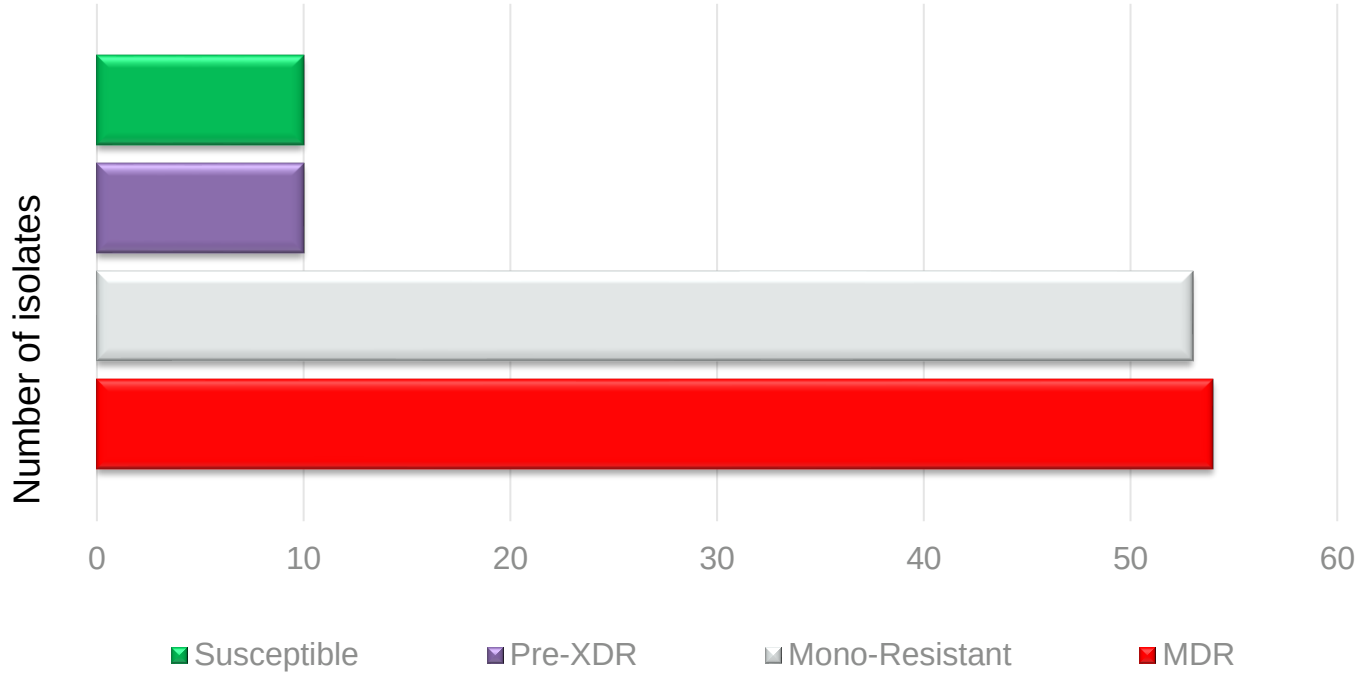


Fig.1. Methods used in this study

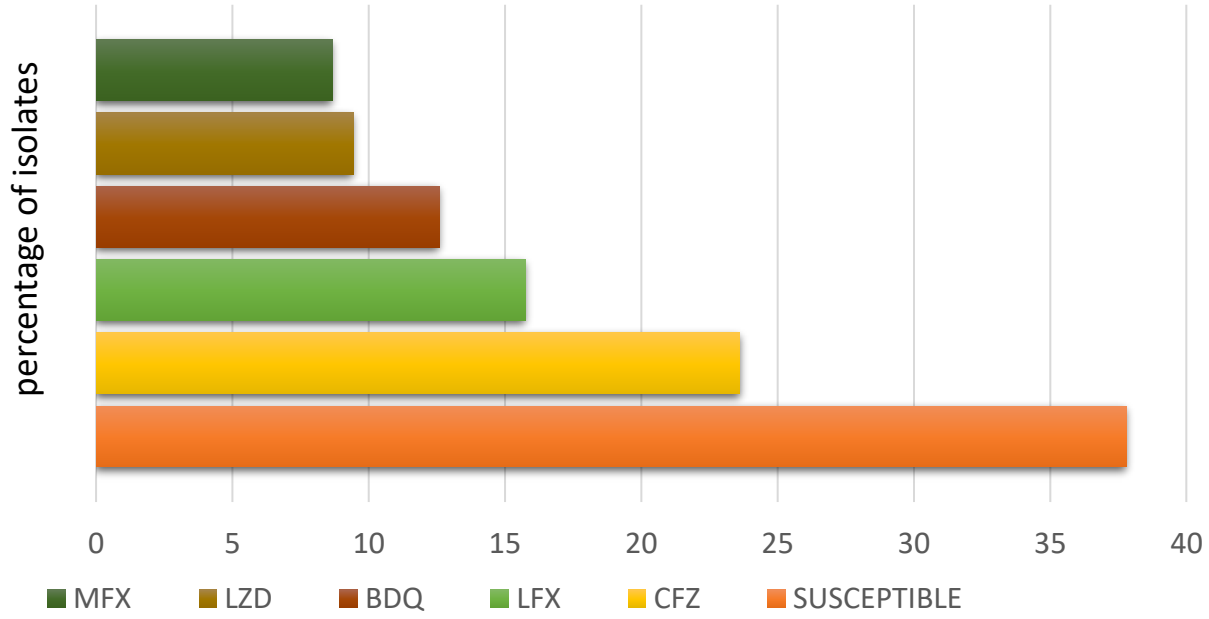
RESULTS



- Total =127 MTB samples
  - 10 susceptible
  - 54 MDR
  - 53 mono resistant
  - 10 preXDR

Fig.2. Drug resistance profile of isolates

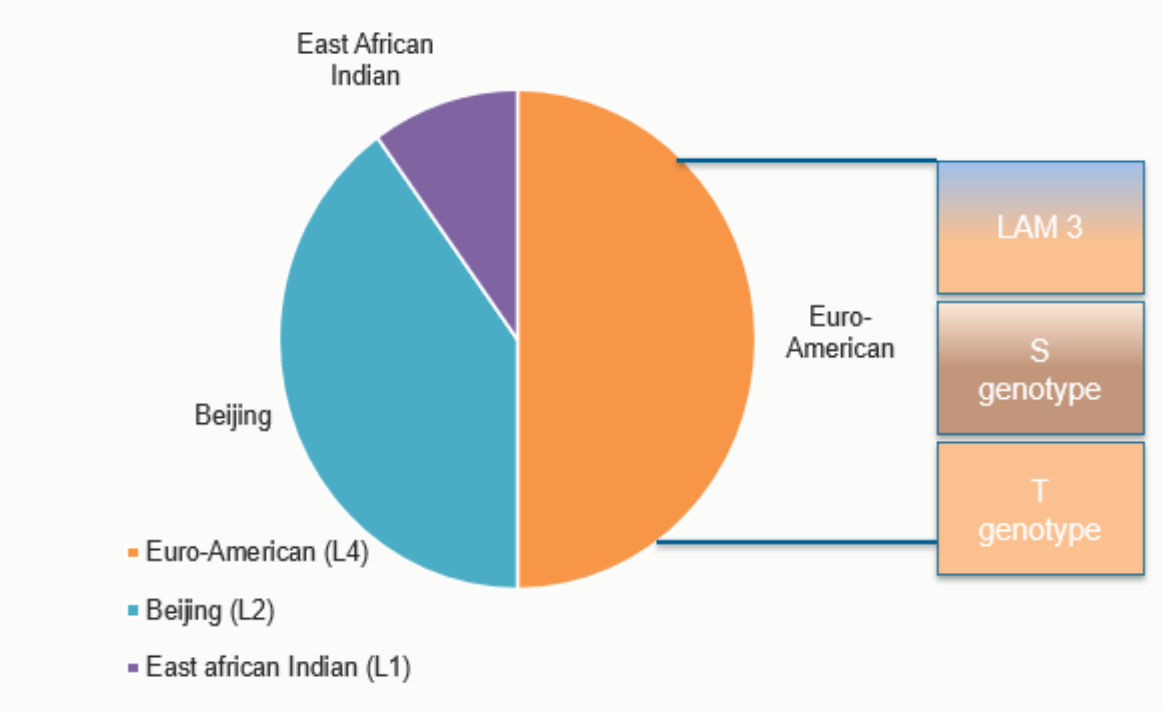
RESULTS



- 37.79% of isolates were susceptible to second-line drugs
- CFZ resistance was the most predominant (23.62%)
- MFX was the least 8.66%

Fig.3. Second line phenotypic drug susceptibility testing (DST)

RESULTS

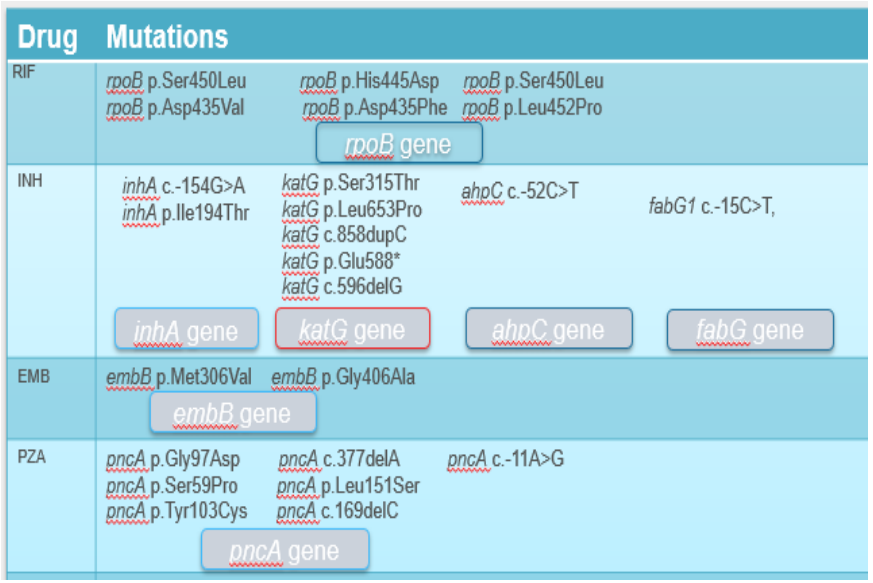


Lineage/drug-resistance

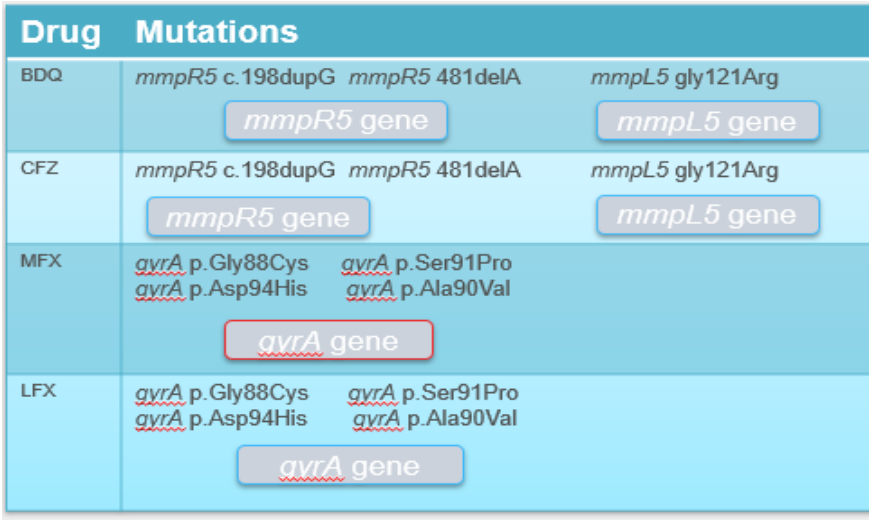
- All were drug-resistant strains
- East African Indian (EAI) : pre-XDR
- Euro- American:
  4 = MDR-strain
  1 = pre-XDR
- Beijing: 3 = MDR
  1 = pre-XDR

Fig.4. Lineage distributions and association between lineages vs drug-resistance

First-line TB drugs



Second line-line TB drugs



Drug resistant determinates

Anti-TB drugs	Total number of mutations per drug	Associated with resistance	Uncertain confidence	Not associated
Rifampicin	72	6	27	39
Isoniazid	53	9	35	9
Bedaquiline	31	3	17	11
Clofazimine	31	3	17	11
Moxifloxacin	31	4	15	12
Levofloxacin	31	4	15	12
Linezolid	8	-	2	6
Total	**195**	**22**	**118**	**77**

CONCLUSION

- This is a preliminary results of the ongoing study that seek to identify mutation determinants that will be used develop a bioinformatics tool for MTB diagnosis *as* well as detection of drug-resistance and lineages
- Our study detected two dominant global lineages L2 and L4; most prevalent in South Africa, associated with drug resistant
- Most of our isolates were collected from Mpumalanga, Gauteng and North West, known for industrial activities, overcrowding and mining respectively
- May be contributor to genetic diversity and development of drug resistance
- We anticipates that WGS has the potential to significantly accelerate the detection of drug resistance profiles compared to phenotypic DST methods.
- Identifying and understanding mutations conferring drug-resistance and genetic diversity of MTB will help

  1. To eradicate TB transmission and outbreaks 2. Preserve current drugs and developing new potent drugs 3. Develop diagnostic tool that accelerate the existing progress to end TB

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THANK YOU