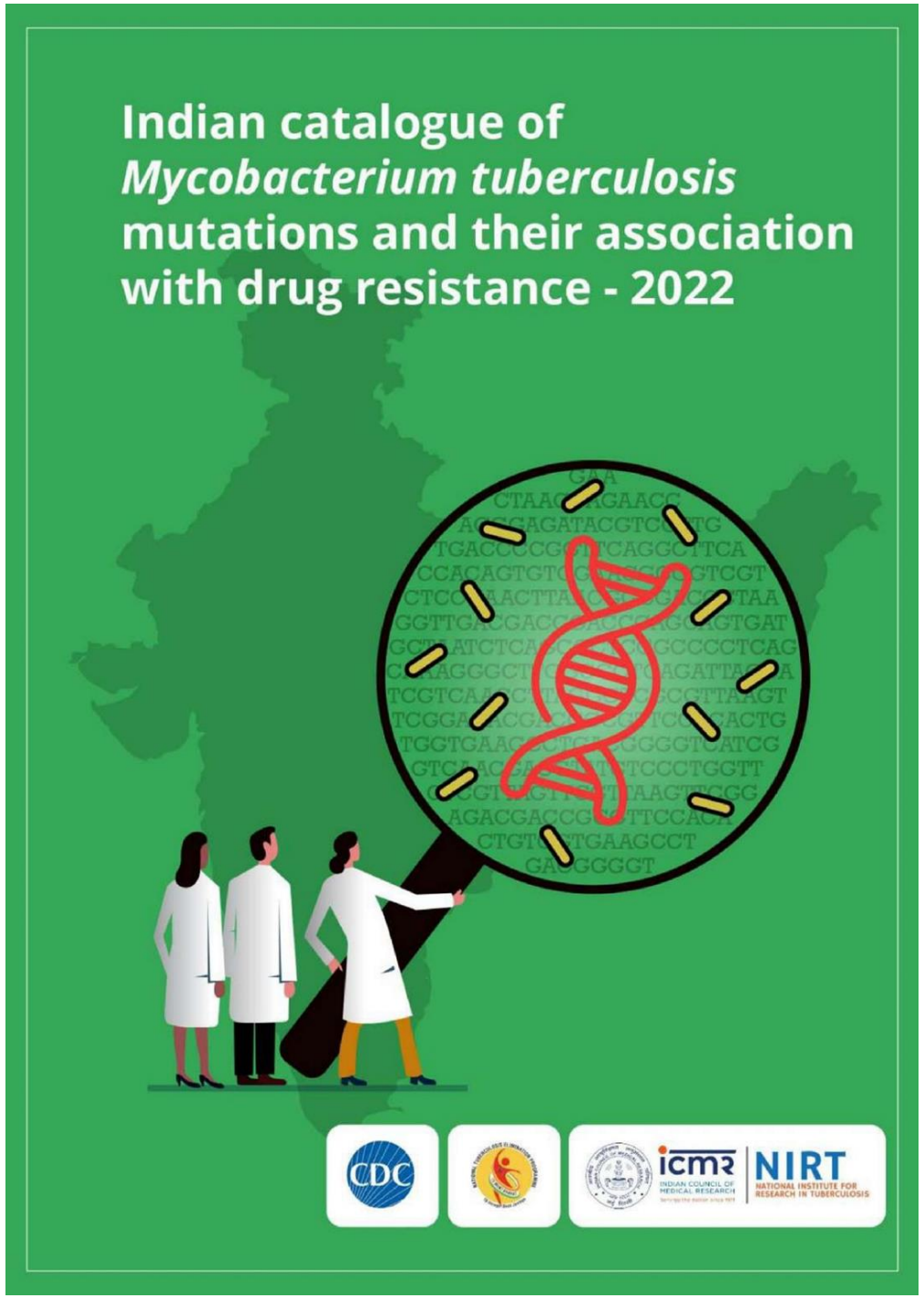

Indian Catalogue of Mycobacterium tuberculosis Mutations and their Association with Drug Resistance - 2022

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Understanding the Indian Catalogue of MTB Mutations

Background:

- MTB genotypes are not evenly distributed around the globe**.**
- The Indian Catalogue of Mycobacterium tuberculosis Mutations and their Association with Drug Resistance - 2022 provides insights into TB drug resistance in India.
- This catalogue documents MTB-specific mutations graded into five categories of TB drug-resistance association, based on a comparison of genotypic and phenotypic data (WHO endorsed methods - BACTEC MGIT 960 liquid culture and CC) for a large collection of strains collected across India.
- CamNirtRespred - in-house pipeline was used to perform WGS analysis.

Importance:

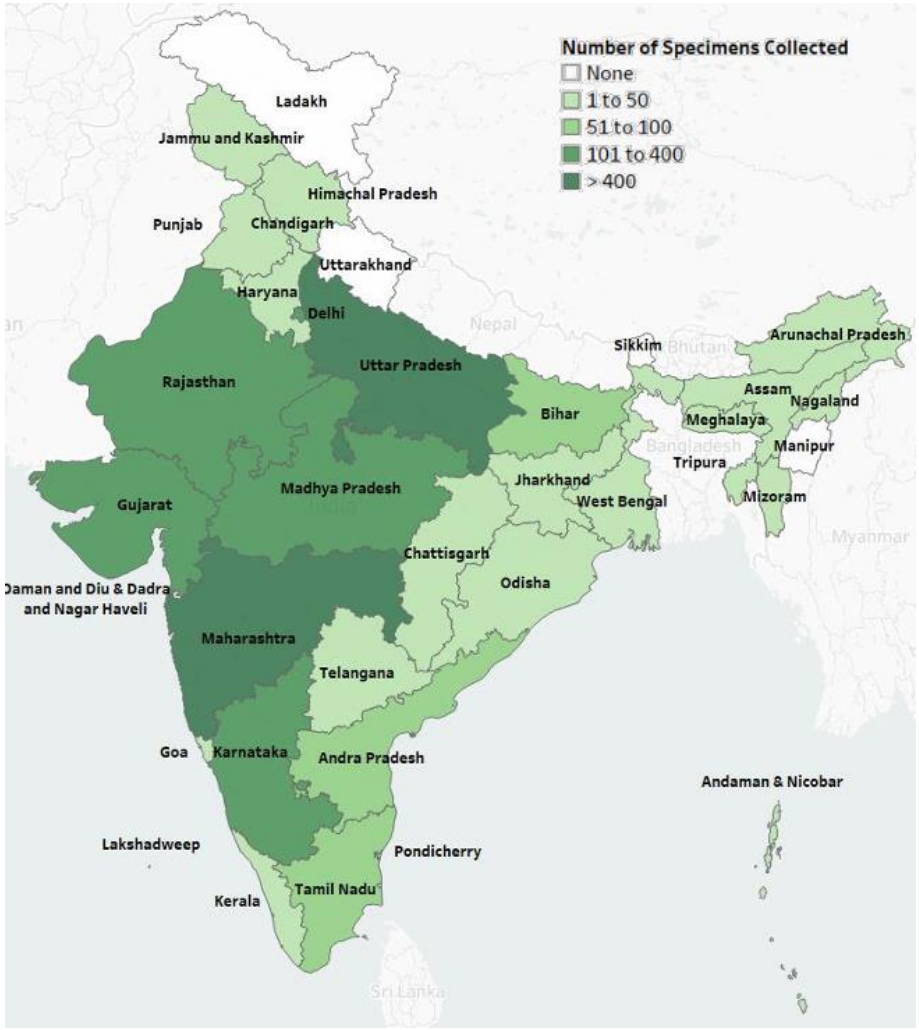
- This catalog serves as a vital resource for understanding drug resistance patterns in TB across different regions of India.

Collaborators:

- Collaboration with Central TB Division (CTD) of India.
- Funding by the US Centers for Disease Control and Prevention

Delving into Mutation Analysis

Figure 1. Geographic distribution of the number of MTBC isolates or processed sputum collected by State and Union Territories – India.



- Quota sampling method utilized to collect 3,167 MTBC isolates from 25 States and 4 Union Territories (2018-2021).
- 2,112 isolates selected for downstream analysis based on quality genotypic and phenotypic drug susceptibility testing data.
- A comprehensive set of mutations and their association with resistance to 15 anti-TB drugs was catalogued.
- 8,825 mutations queried based on the 2021 WHO Mutations Catalogue approach.
- Initial grading resulted in 45 mutations classified into Group 1 and 118 mutations into Group 2.
- Expert rules application led to an additional 520 mutations placed within Group 2, totaling 683 mutations associated with resistance.

New and Repurposed Drugs

Table 1. Mutations identified in genes associated with resistance to BDQ.

S. No	pDST	gDST (WGS) Mutations	Gene/ RvID
1	Susceptible	D88G	Rv0678
2	Susceptible	V1A	Rv0678
3	Susceptible	S53L	Rv0678
4	Susceptible	A59V	Rv0678
5	Susceptible	G11G	Rv0678
6	Resistant	R50W	Rv0678
7	Resistant	T33A	Rv0678
8	Resistant	I66M	*atp*E/ Rv1305
9	Susceptible	D15G	Rv0678
10	Susceptible	S52F	Rv0678
11	Resistant	S53P	Rv0678
12	Susceptible	I108T	Rv0678

•11 non-synonymous mutations in transcriptional repressor Rv0678 linked to BDQ resistance (T33A, R50W I66M & S53P are linked to phenotypic BDQ resistance).

•T33A is unique to India dataset (It was not reported in WHO cat. **version 1** & **2**).

•S53P in Rv0678 was reported in WHO cat. **ver 2** as group 3 mutation (it was not reported in **ver 1**).

•R50W in Rv0678 was reported in WHO cat. **ver 1** as group 3 (it was not reported in **ver 2**).

•Mutation in *atpE* (I66M) linked to phenotypic BDQ resistance discovered in the dataset was reported in WHO cat. **ver 2** (it was not reported in **ver 1**).

•27 isolates carrying LZD resistance C154R mutation in rplC, graded as Group 1 in both versions 1 and 2 of the WHO catalogue, exhibited resistance by pDST..

•The LZD-resistant mutation in rrl (g2814t) reported in the Indian catalogue (as Group 3) was initially classified as Group 3 in WHO catalogue ver 1, but has now been reclassified as Group 2 in ver 2.

Evolving Insights and Significance

Future Outlook:

- As more strains are analyzed, mutations currently in Groups 3, 4, and 5 may transition to Groups 1 or 2, enhancing our understanding of drug resistance mechanisms.
- Indian Mutation Catalogue version 2 is under development.

Data Impact:

- Increased data inclusion enables more robust analysis, refining our interpretation of mutation groups and their implications for TB drug resistance.

Practical Application:

- This standardized resource is invaluable for guiding national efforts in TB surveillance and disease control, aiding in the development of targeted interventions and treatment strategies.

Study Team

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THANK YOU