DEEPLEX

Deeplex® Myc-TB

From clinical samples to drug resistance profile

SAMPLE REPORT

January 2021– V1

CE IVD

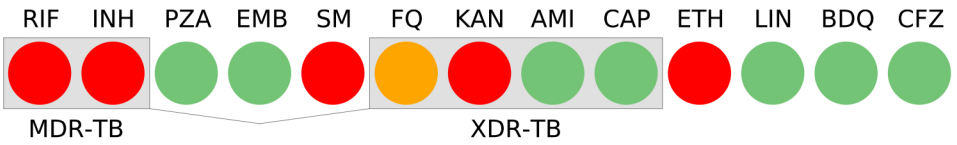
GenoScreen
Innovative Genomics

GenoScreen
Innovative Genomics

DEEPLEX® Myc-TB Report

XDR (Extensively Drug Resistant) MTBC sample

Date of submission	**Jan, 12 2021 11:08:09**
Analysis mode	**Deeplex-2.0.2**
Quality	⊕⊕



Legend [1]

Sample controls and metrics[2]

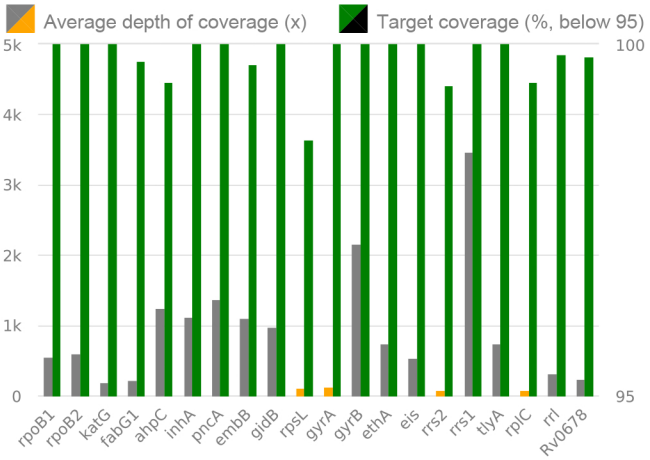
Sequencing Run:

Positive control*	**VALID**
Negative control*	**VALID**

Sample:

Internal control*	**VALID**
Composite reference coverage	**99.955%**
Median depth of coverage*	**728x**

(min. rplC: 82x; max. rrs1: 3471x)



hsp65-based species identification

Av coverage depth (x)	Consensus length	% Identity	E-value	Best match
77.6	399.0	100.000	0.0	*Mycobacterium tuberculosis* complex

Drug resistance associated variants[3]

Gene	Genomic position	Codon change	% Variant	Dx-score	AA change	Drug*	Confidence	Resistance level	PMID
eis	2715342	G-10A	100.000	137.00	n/a	KAN	High	Resistant	ReSeqTb
ethA	4327147	TGG109TGA	99.864	184.25	W109Stop	ETH	n/a	Resistant	n/a
gyrA	7570	GCG90GTG	28.966	10.50	A90V	FQ	High // High	Intermediate	ReSeqTb
katG	2155168	AGC315ACC	100.000	20.25	S315T	INH	High	Resistant	ReSeqTb
rpoB	761155	TCG450TTG	100.000	137.00	S450L	RIF	High	Resistant	ReSeqTb
rpsL	781687	AAG43AGG	100.000	31.00	K43R	SM	High	Resistant	ReSeqTb

Uncharacterized variants[3]

Uncharacterized variants designate sequence variants of as yet unknown association with drug sensitivity or resistance.

No uncharacterized variants detected in any gene target.

Spoligotype

Octal code/ Binary code	Av. coverage depth (x)	SIT	SITVIT occurence	Clade
000000000000031	13.3	585	8	Beijing
00000000000000000000000000000000000000000111				

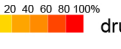
SNP-based phylogenetic lineage

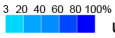
Lineage 2 (*M. tuberculosis*)

Potential mixed infection

Mixed infection is signaled by a phylogenetic variant detected at less than 97%, indicating the simultaneous presence of 1 strain harboring this variant present at this percentage and another strain sharing the same sequence as the reference at this position, present at approx. 100% minus this percentage.

Not detected.

[1] Deeplex map: the circular map is divided in 13 “sectors” associated with 13 drugs or drug classes. Sectors are colour-coded as follows: 

drug resistance-associated variants (or indels) detected in gene target with percent subpopulation according to colouring; 

uncharacterized variants (or indels) detected in gene target with percent subpopulation according to colouring; no variant or indel detected in gene target or only variants or indels unrelated to drug resistance; suboptimal gene target coverage; nontuberculous *Mycobacterium* (NTM) identified.
Detected variants or indels are specified by codon, amino acid or nucleotide changes (deletions shown as *) on the outermost part, using the same colour codes as above for drug resistance-associated and uncharacterized categories, or in grey ( ) for variants or indels unrelated to drug resistance. Target reference sequences are coloured according to gene target coverage as follows: coverage >95%, coverage <95%. Limit of detection histogram for each target is colour-coded as follows: 1% ≤ limit of detection of 3%, 3% < limit of detection ≤ 80%.

Resistotype: First-line drugs: rifampicin (RIF), isoniazid (INH), pyrazinamide (PZA), ethambutol (EMB). Second-line injectables: Streptomycin (SM), kanamycin (KAN), amikacin (AMI), capreomycin (CAP); fluoroquinolone class (FQ) includes levofloxacin (LEV), ofloxacin (OFX) and moxifloxacin (MOX); ethionamide (ETH); linezolid (LIN); bedaquiline (BDQ); clofazimine (CFZ). MDR-TB, multidrug-resistant TB defined as resistance to at least rifampicin and isoniazid. XDR-TB, extensively drug-resistant TB defined as MDR-TB plus resistance to at least one fluoroquinolone and a second-line injectable.

[2] Positive control: valid if identified as *Mycobacterium tuberculosis* complex with spoligotype SIT 482, lineage *Mycobacterium bovis* BCG and 9 expected mutations detected at >99% and no other mutations detected at >5%; Negative control: composite reference coverage breadth <40% (far below minimal coverage considered for identification and resistance prediction); Internal control: valid if average coverage depth >100x and coverage breadth >95% on internal control, and average coverage depth <100x over the other targets; Composite reference coverage: coverage breadth over the concatenated reference sequences associated with drug resistance; Median depth of coverage: median of average read depths among reference sequences associated with drug resistance; (min x, max x): minimal/maximal average coverage depth among the targets

[3] **Dx-score** designates the excess of coverage depth at the variant position, relative to the minimal coverage depth required to detect the observed percent of variant. Minimal value is 1. * Antibiotics highlighted in graded colours according to percent of drug resistance associated or uncharacterized variant detected (see colour grades above).

[4]OFX is not used for the treatment of *Mycobacterium tuberculosis* although potential resistance to OFX is tested, as part of the Fluoroquinolones

Disclaimer

Resistance is reported when a documented resistance-conferring mutation is detected in targets of interest*. **The absence of detected mutations does not exclude the possibility of resistance.** Low-frequency hereteroresistance below the limit of detection by sequencing may affect typing results. The interpretation provided is based on the current understanding of genotype-phenotype relationships. All results reference the *M. tuberculosis* mutation numbering system, which differs from *Escherichia coli* numbering system.

* Resistance-conferring mutations documented in ReSeqTB Data Platform, Miotto P. *et al.* Eur Resp J 2017, Miotto P. *et al.* mBio 2014, PhyResSE (Feurriegel *et al.* J. Clin. Microbiol. 2015), Walker *et al.* Lancet. Infect. Dis. 2015.

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