Diagnosi MDR/XDR 2019 e allineamento con la terapia

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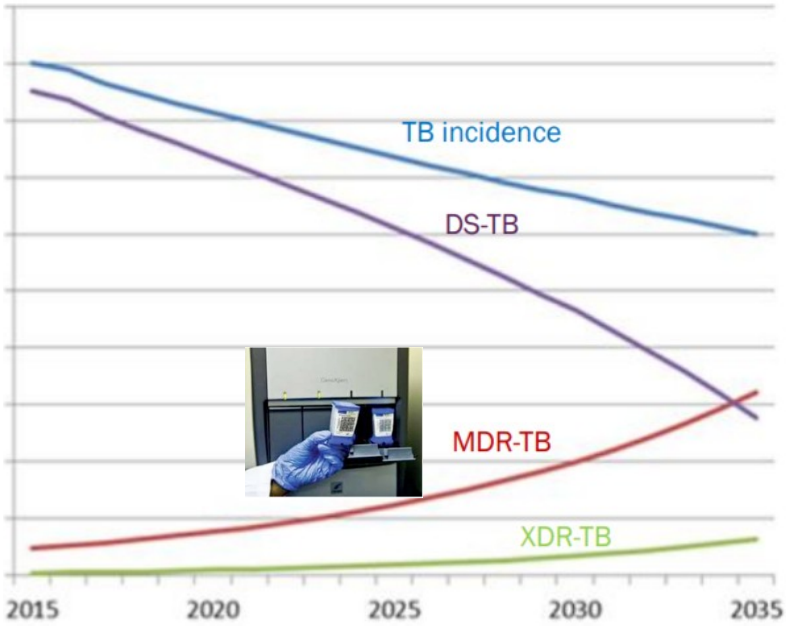
Emerging Bacterial Pathogens Unit,
San Raffaele Scientific Institute, Milan

SOMMARIO

- Diagnosi MDR/XDR Problematiche legate alle nuove raccomandazioni sulla terapia
- Uso dei test molecolari: rischi e benefici
- WGS/NGS perchè è meglio
- Nuovi farmaci: come effettuare la sorveglianza
- Trasmissione e analisi dei clusters

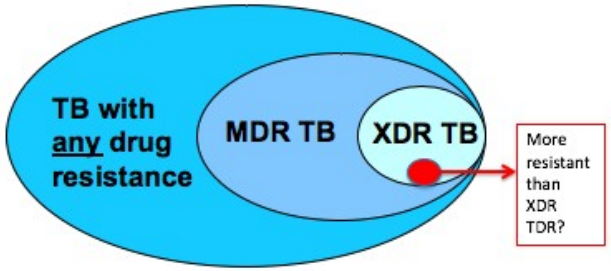
MDR-TB and diagnostic gaps



Only 20% MDR cases diagnosed or treated: 448,000 of 580,000 MDR cases missed

MDR TB = Strains resistant to at least INH and RIF (most important 1st-line drugs)

XDR TB = *MDR TB strains with additional resistance to any fluoroquinolone and any of the 3 injectable second-line drugs (amikacin, kanamycin, capreomycin)*



Opzioni terapeutiche

- Short regimen (9 mesi)
- Regime personalizzato

Criteria under which the shorter MDR-TB regimen may be offered

Any of the following conditions present?

- *Preference by the clinician and patient for a longer MDR-TB regimen*
- Confirmed resistance or suspected ineffectiveness to a medicine in the shorter MDR-TB regimen (except isoniazid resistance)
- Exposure to one or more 2nd line medicines in the shorter MDR-TB regimen for >1 month (*unless susceptibility to these 2nd line medicines is confirmed*)
- Intolerance to medicines in the shorter MDR-TB regimen or risk of toxicity (e.g. drug-drug interactions)
- Pregnancy
- *Disseminated, meningeal or central nervous system TB*
- *Any extrapulmonary disease in PLHIV*
- One or more medicines in the shorter MDR-TB regimen not available

FAILING SHORTER REGIMEN or NON-RESPONSE, DRUG INTOLERANCE, EMERGENCE OF ANY OTHER EXCLUSION CRITERION

YES → **New, individualized longer MDR-TB regimens**

NO → **Standardized, shorter MDR-TB regimen** may be offered (conditional recommendation)

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Revisione del regime lungo/personalizzato

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World Health Organization

Rapid Communication:
Key changes to treatment of multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB)

August 2018

GROUP	MEDICINE	Abbreviation
Group A: Include all three medicines (unless they cannot be used)	Levofloxacin OR Moxifloxacin	Lfx Mfx
	Bedaquiline[1,4]	Bdq
	Linezolid[2]	Lzd
Group B: Add both medicines (unless they cannot be used)	Clofazimine	Cfz
	Cycloserine OR Terizidone	Cs Trd
Group C: Add to complete the regimen and when medicines from Groups A and B cannot be used	Ethambutol	E
	Delamanid[3,4]	Dlm
	Pyrazinamide[5]	Z
	Imipenem-cilastatin OR Meropenem[6]	Ipm-Cln Mpm
	Amikacin (OR Streptomycin)[7]	Am (S)
	Ethionamide OR Prothionamide	Eto Pto
	p-aminosalicylic acid	PAS

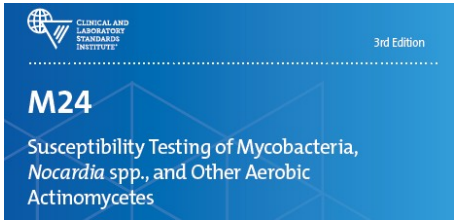
- Kanamycin and capreomycin are no longer in the regimen to treat MDR/RR-TB;
- Bedaquiline and linezolid have been upgraded and prioritized;
- All oral
- In the shorter regimen for MDR/RR-TB, kanamycin and capreomycin should be replaced with amikacin (or bedaquiline under operational research conditions).

2018

Technical Report on
critical concentrations for drug susceptibility testing of medicines used in the treatment of drug-resistant tuberculosis

World Health Organization

FIND


CLINICAL AND LABORATORY STANDARDS INSTITUTE

3rd Edition

M24

Susceptibility Testing of Mycobacteria, *Nocardia* spp., and Other Aerobic Actinomycetes

Improper use of diagnostics is not “risk free”

- Xpert MTBrif has revolutionized the detection of MDR-TB allowing detection of cases to be started on treatment
- Test detects with high sensitivity the Tb genomes and detect mutations in a DNA fragment of 88bp in *rpoB* responsible for 95% of RR cases

Solo un'analisi comprensiva del genoma o la MIC permettono una decisione su dosaggio

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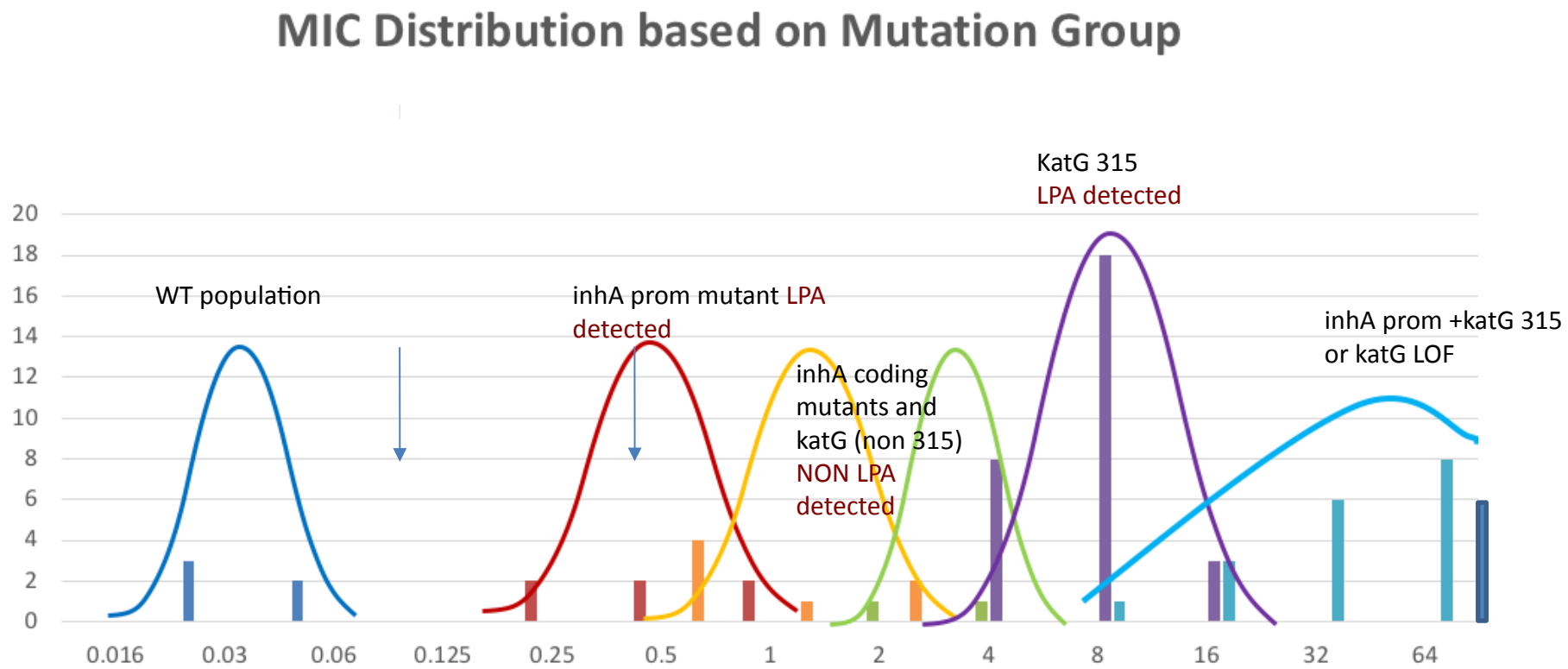


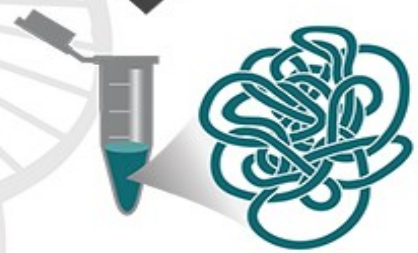
Ghodousi A. submitted 2019.

The Whole Genome Sequencing (WGS) Process

WGS is a laboratory procedure that determines the order of bases in the genome of an organism in one process. WGS provides a very precise DNA fingerprint that can help link cases to one another allowing an outbreak to be detected and solved sooner.

1. DNA Extraction

1 Scientists take bacterial cells from an agar plate and treat them with chemicals that break them open, releasing the DNA. The DNA is then purified.



2. DNA Shearing

2 DNA is cut into short fragments of known length, either by using enzymes "molecular scissors" or mechanical disruption.

3. DNA Library Preparation

3 Scientists make many copies of each DNA fragment using a process called polymerase chain reaction (PCR). The pool of fragments generated in a PCR machine is called a "DNA library."

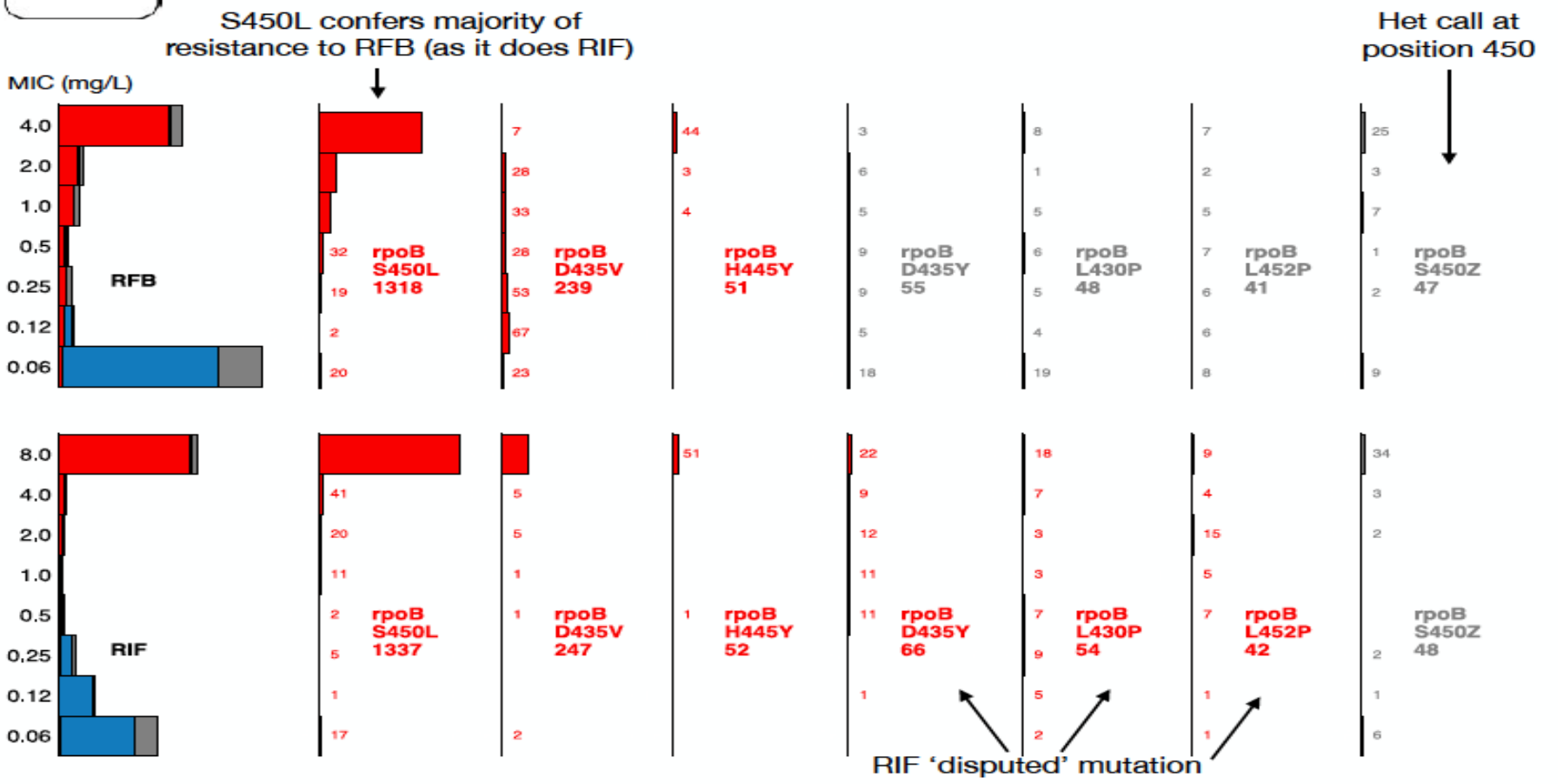
4. DNA Library Sequencing

4 The DNA library is loaded onto a sequencer. The combination of nucleotides (A, T, C, and G) making up each individual fragment of DNA is determined, and each result is called a "DNA read."

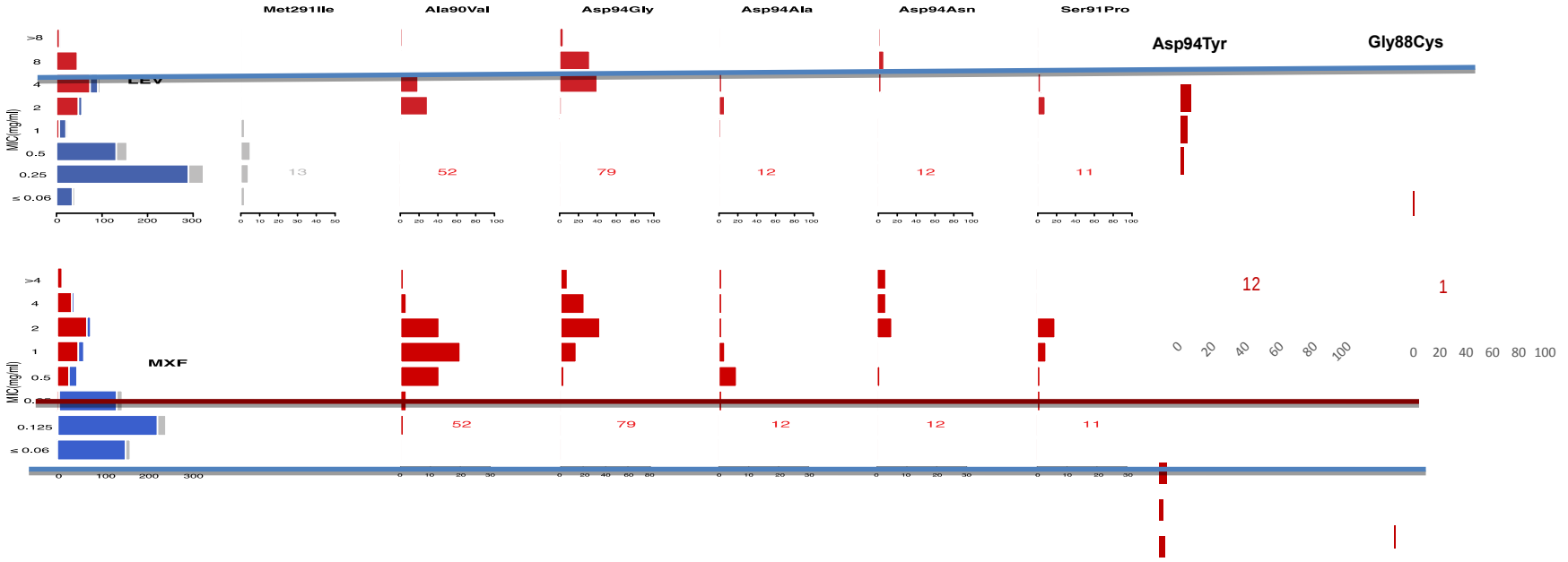
5. DNA Sequence Analysis

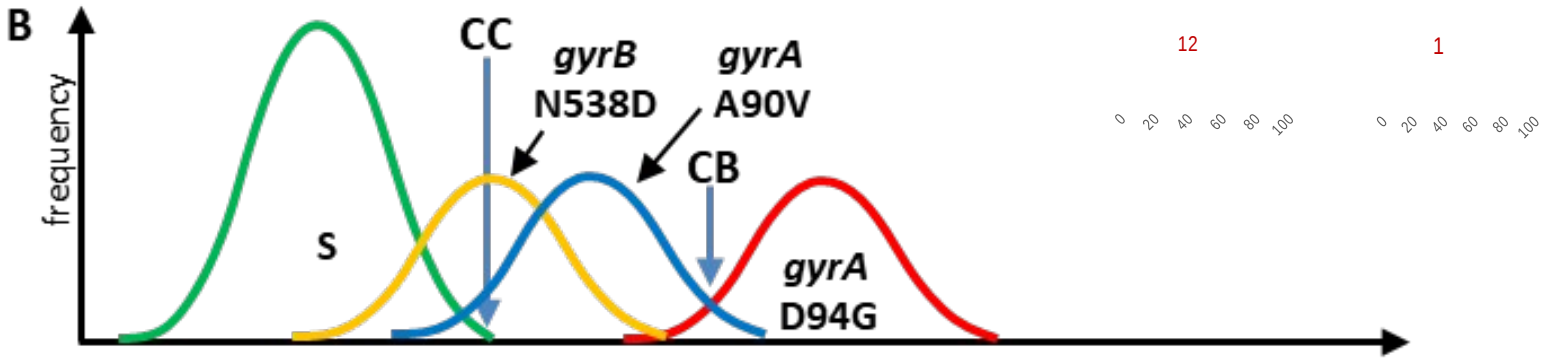
5 The sequencer produces millions of DNA reads and specialized computer programs are used to put them together in the correct order like pieces of a jigsaw puzzle. When completed, the genome sequence containing millions of nucleotides (in one or a few large pieces) is ready for further analysis.

Beginning to see subtle RFB/RIF differences…



Fluoroquinolones: high vs low level of resistance





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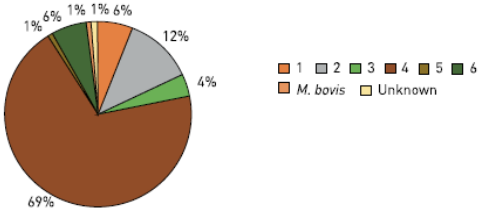
AGOI RESEARCH LETT

Study collection at RCM (February 2016–September 2017)	
Isolates collected in the study period (20 months) n	328
Isolates tested by WGS in the study period n	298 (91%)
Unique cases enrolled with WGS available in the study period n	285
Unique cases with MDR-TB n	11
Unique cases with XDR-TB n	1

Diagnostic performance of WGS for diagnosis of resistance to first-line anti-TB drugs (*versus* MGIT)[#,¶]

Drug/pattern	Sensitivity		Specificity		PPV	NPV
	Resistant isolates n	% (95% CI)	Susceptible isolates n	% (95% CI)	% (95% CI)	% (95% CI)
RIF-R	12*	100 (75.75–100)	272	99.63 (97.95–99.94)	92.31 (66.69–98.63)	100 (98.6–100)
INH-R	31	100 (88.97–100)	254	100 (98.51–100)	100 (88.97–100)	100 (98.51–100)
PZA-R	24	62.5 (42.71–78.84)	261	99.62 (97.86–99.93)	93.75 (71.67–98.89)	96.65 (93.76–98.23)
ETB-R	10	90 (59.58–98.21)	275	98.55 (96.32–99.43)	69.23 (42.37–87.32)	99.63 (97.95–99.94)
MDR	12	100 (75.75–100)	272	99.63 (97.95–99.94)	92.31 (66.69–98.63)	100 (98.6–100)

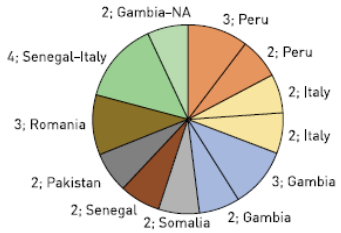
WGS-based *M. tuberculosis* complex genotyping [§]: lineage distribution

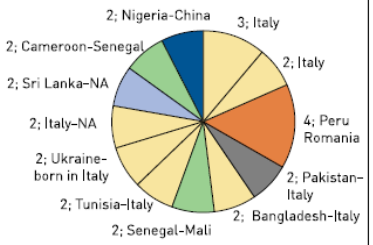


cgMLST outbreak analysis (*versus* contact tracing)[ƒ,##]

Transmission	Confirmed by contact tracing			Not confirmed by contact tracing or information not available		
	Isolates n	Independent events n	% on clustered patients (n=56)	Isolates n	Independent events n	% on clustered patients (n=56)
	29	12	51.78	27	12	48.21

By nationality (number of patients in cluster; patient origin):





	Isolates n	Independent events n	% on total isolates (n=298)
Laboratory cross-contamination	11	7	3,69
Second isolate from the same person ¶¶	13	12**	4,36

Countrywide implementation of whole genome sequencing: an opportunity to improve tuberculosis management, surveillance and contact tracing in low incidence countries

Andrea Maurizio Cabibbe[1], Alberto Trovato[1], Maria Rosaria De Filippo[1], Arash Ghodousi[1], Laura Rindi[2], Carlo Garzelli[2], Simonetta Baretti[3], Guendalina Allodi[3], Roberta Mannino[4], Gian Maria Rossolini[4,5], Alessandro Bartoloni[5,6], Enrico Tortoli[1] and Daniela Maria Cirillo[1]

- Based on early MGIT culture
- Statistically significant decrease in time to results
- Additional relevant data:
  - Transmission
  - Laboratory cross-contamination

Building the framework for standardized clinical laboratory reporting of next generation sequencing data for resistance-associated mutations in *Mycobacterium tuberculosis* complex

Jeffrey A. Tornheim,[1‡] Angela M. Starks,[2‡] Timothy C. Rodwell,[3,4] Jennifer L. Gardy,[5,6] Timothy M. Walker,[7] Daniela Maria Cirillo,[8] Lakshmi Jayashankar,[9] Paolo Miotto,[8] Matteo Zignol,[10] Marco Schito[11]

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2a. One-Page Report

Barcode XXXXXXXXXXXX

MYCOBACTERIUM TUBERCULOSIS SEQUENCING REPORT

Sample Details

Patient Name	JOHN DOE	Patient ID	12345678910
Birth Date	2000-JAN-01	Location	SOMEPLACE
Sample Type	SPUTUM	Sample Collection Date	2016-DEC-25
Sample Source	PULMONARY	Sequenced From	CULTURED ISOLATE (LJ)
Sample ID	A12345678	Sample Received Date/Time	2017-JAN-02, 12:22
Laboratory Technician	TECHNICIAN NAME	Report Date/Time	2017-JAN-05, 11:45
Requested By	REQUESTER NAME	Requester Contact	REQUESTER@EMAIL.COM

Assay Details

Sequencer	ILLUMINA HISEQ 2500	Method	WHOLE GENOME SEQUENCING
Pipeline	RESEQTBV.3.2C (https://platform.reseqtb.org)	Reference	H37RV (NC_000962.3)

Final Result

The sample was positive for ***Mycobacterium tuberculosis***.
It is **resistant to isoniazid, rifampin, capreomycin, kanamycin, ofloxacin, and moxifloxacin.**

Lineage

Mycobacterium tuberculosis, lineage 2.2.1 (**East-Asian Beijing**).

Drug Susceptibility

Resistance is reported when a high likelihood resistance-conferring mutation is detected in loci of interest.[1] **No mutation detected does not exclude the possibility of resistance.**

☐ No mutations detected
☐ Multi-drug resistance predicted
☑ **Extensive drug resistance predicted**

	Interpretation	Drug	Gene Target (Mutation, Allele %)	Comments
First Line	Resistant	Isoniazid	*katG* (Ser315Thr, 100%)	
		Rifampin	*rpoB* (Ser450Leu, 100%)	Rifabutin resistance likely
	Susceptible	Ethambutol		No mutation detected
		Pyrazinamide		***Expert consultation advised***
Second Line	Resistant	Capreomycin	*rrs* (C1402T, nucleotide 100%)	At least low-level resistance predicted
		Kanamycin	*rrs* (C1402T, nucleotide 100%)	
		Moxifloxacin	*gyrA* (Ala90Val, 14%)	
		Ofloxacin	*gyrA* (Ala90Val, 14%)	
	Susceptible	Amikacin		No mutation detected
		Ethionamide		No mutation detected
		Streptomycin		No mutation detected

Disclaimer

[1]Loci of interest derived from ReSeqTB Data Platform and from Miotto P, et al. Eur Respir J. 2017 PMID: 29284687
Low frequency hetero-resistance 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 the *E. coli* numbering system.

Authorized By

Name	AUTHORIZER NAME	Position	LAB SUPERVISOR
Signature		Date	2017-JAN-05
Reporting Laboratory	LAB NAME	LAB ADDRESS	LAB PHONE NUMBER

2b. Long Report Resistance Prediction

Resistance Predictions for First Line TB Drugs

Interpretation	Drug	Gene Target (Codon Change, Amino Acid Change, Allele %)	Confidence in Resistance Association	Comments
Resistant	Isoniazid	*katG* (G944C, Ser315Thr, 100%)	High	
		inhA		No mutation detected
		mshA		No mutation detected
	Rifampin	*rpoB* (C1349T, Ser450Leu, 100%)	High	Rifabutin resistance likely
Susceptible	Ethambutol	*embB*		No mutation detected
	Pyrazinamide	*pncA* (T416C, Val139Ala, 98%)	Minimal	Mutation known to disrupt enzymatic activity and functional genetics in vitro. Insufficient data to determine clinical impact of this mutation.

2c. Long Report NGS Statistics

Depth and Coverage Details

Locus of Interest[1]	# Reads Mapped (Depth of Coverage)	Proportion Covered (Coverage Width %)	*Mutation Frequency (% Alternate Allele)*
atpE	79	100	-
ddn	97	99.9	-
embB	88	98.8	-
fbiA	87	100	-
fbiB	91	100	-
fbiC	75	100	-
fgd1	88	100	-
gyrA	73	100	Ala90Val (13.6%*)
gyrB	76	100	-
inhA	91	100	-
katG	90	99.9	Ser315Thr (1
mmpR	62	100	G193Insertion (
pncA	62	100	Val139Ala (9
rplC	78	99.9	Cys154Arg (9
rpoB	83	100	Ser450Leu (1
rrf	82	100	-
rrs	59	99.9	C1402T (96.6%)
tlyA	58	98.5	-

*Hetero-resistance is defined in this report as a proportion of reads for a given allele between 10% and 90%.
[1]Loci of interest derived from ReSeqTB Data Platform and from Miotto P, et al. Eur Respir J. 2017 PMID: 29284687

ReSeqTB
Relational Sequencing TB Data Platform

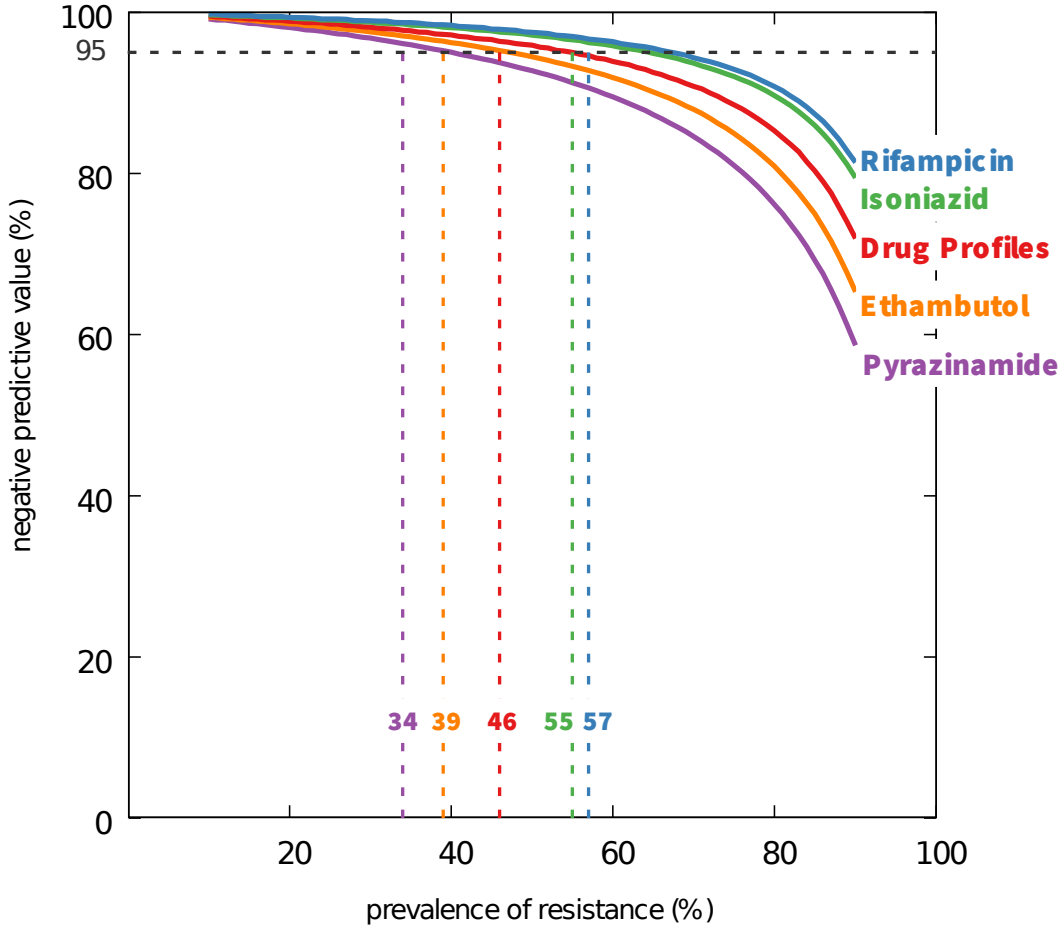
"Can we already predict enough *Mtbc* phenotypes from routinely produced WGS data, with sufficient accuracy, to justify a substantial reduction in phenotyping activity?"

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prediction of Susceptibility to First-Line Tuberculosis Drugs by DNA Sequencing

The CRyPTIC Consortium and the 100,000 Genomes Project



Il valore Predittivo Negativo è superiore al 95% anche a livelli di prevalenza delle resistenze molto alti

NGS based target screening da campione diretto BAAR+

Mycobacteria ID species (hsp65, rrs, rplC, rrl)

Spoligotyping

CRISPR/DR region

Phylogenetic SNPs

Rifampicin	rpoB
Isoniazid	inhA, fabG1, katG, ahpC
Ethionamide	ethA, inhA
Pyrazinamide	pncA
Ethambutol	embB
Streptomycin	rpsL, rrs, gidB
Amikacin	rrs
Kanamycin	rrs, eis
Capreomycin	rrs, tlyA
Fluoroquinolones	gyrA, gyrB
Linezolid	rrl, rplC
Bedaquiline	Rv0678
Clofazimine	Rv0678

Mutations detected with Deeplex Myc TB assay	Mutations detected with WGS on corresponding isolates: Mutation detected	No mutations	Performance (% [95%CI*]): Correlation	Sensitivity	Specificity
INH					
Mutation detected	5	0	100 (95.3 - 100)	100 (56.6 - 100)	100 (95 - 100)
No mutations	0	73			
RIF					
Mutation detected	4	1[a]	98.7 (93.1 - 99.8)	100 (51.0 - 100)	98.7 (92.7 - 99.8)
No mutations	0	73			
PZA					
Mutation detected	1	3[b]	96.2 (89.3 - 98.7)	100 (20.7 - 100)	96.1 (89.2 - 98.7)
No mutations	0	74			
AMK / KAN					
Mutation detected	3	0	100 (95.3 - 100)	100 (43.9 - 100)	100 (95.1 - 100)
No mutations	0	75			
CAP					
Mutation detected	7	0	100 (95.3 - 100)	100 (64.6 - 100)	100 (94.9 - 100)
No mutations	0	71			
MOX					
Mutation detected	0	1[c]	98.7 (93.1 - 99.8)	na	98.7 (93.1 - 99.8)
No mutations	0	77			

a One sample had a mixture with 2,3% resistant at Ser450Leu
b Three samples had a mixture with <7% resistant mutations
c One sample had a mixture with 6,3% resistant at Asp94Ala

Tagliani E et al , Sci Rep. 2017 Dec 15;7(1):17672

Increase the knowledge to be able to grade and interpret the majority of variants to **new drugs**

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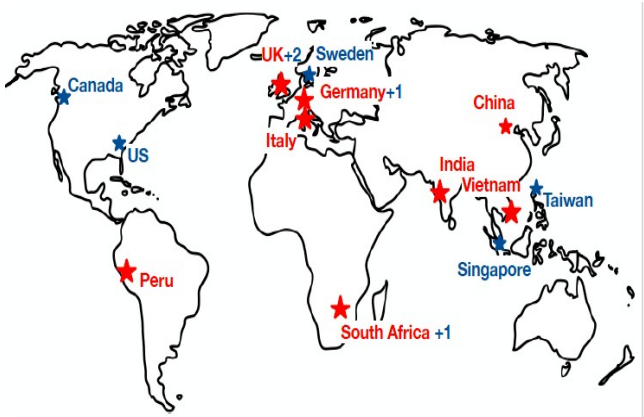
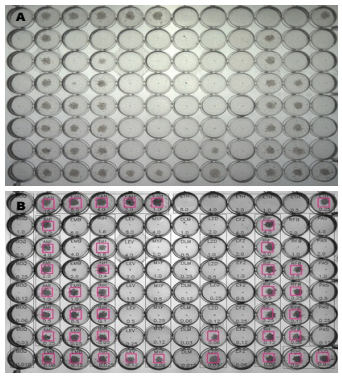
CRyPTIC

wellcome trust | Newton Fund

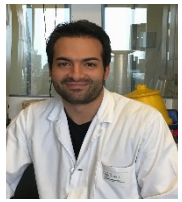
MRC Medical Research Council | BILL & MELINDA GATES foundation





Custom made Microtitre plates

Illumina sequencing



	Genome ..ATCGCA..	UKMYC5 VZ_BDQMIC,.
China	3	909	287
Germany**	726	–	–
India	72	1,975	170
Peru	34	1,030	54
Italy*	–	810	140
Vietnam***	279	374	306
South Africa	145	744	40
Sweden	11	94	8
Taiwan	–	–	–
TOTAL	**1,227**	**5,936**	**1,005**

In May 2018 we had 4,585 matching samples, an increase of +1,351
Sweden and Taiwan have started contributing data

American Journal of Respiratory and Critical Care Medicine 2017;195:A2114

Clinical Profiles of Linezolid Resistant Tuberculosis Cases in Mumbai

Shashank R. Ganatra , Zarir F. Udwadia , Jai B. Mullerpattan , Radhika A. Banka , Ujjwal Sharma , Priti G. Kambli , Camilla S. Rodrigues ,

Of the 2173 MTB isolates tested for Linezolid susceptibility 45(2.07%) were resistant. Of these 45 patients, 26 were XDR, 18 were pre-XDR and 1 was MDR. Of the 45 samples 41 were pulmonary while 4 were extra-pulmonary including 1 pleural fluid, 1 cerebrospinal fluid and 2 lymph nodes tissues.

- Association with time to treatment with second line drugs
- Association with extension of disease

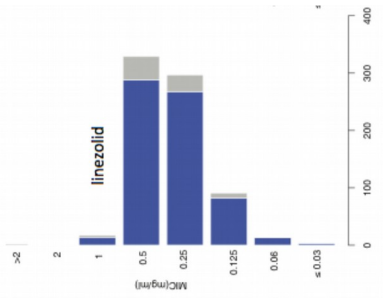
Antimicrob Agents Chemother. 2016 Apr; 60(4): 2542–2544.
Published online 2016 Mar 25. Prepublished online 2016 Jan 25.
doi: 10.1128/AAC.02941-15

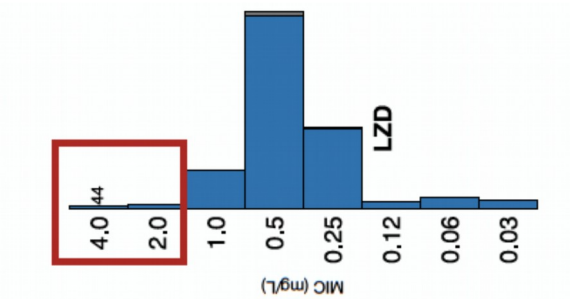
PMCID: PMC4808145
PMID: 26810645

Mycobacterium tuberculosis Mutations Associated with Reduced Susceptibility to Linezolid

Shuo Zhang,[a] Jiazhen Chen,[b] Peng Cui,[b] Wanliang Shi,[a] Xiaohong Shi,[c] Hongxia Niu,[d] Denise Chan,[e] Wing Wai Yew,[e] Wenhong Zhang,[b] and Ying Zhang[a,b]

- Target genes: *rrl* and *rplC* . Mutations in *rplC* are associated with higher MIC values than *rrl* mutations.





Linezolid MICs distribution and correlation with mutations from Cryptic-Italy

Emerging Bacterial Pathogens Unit

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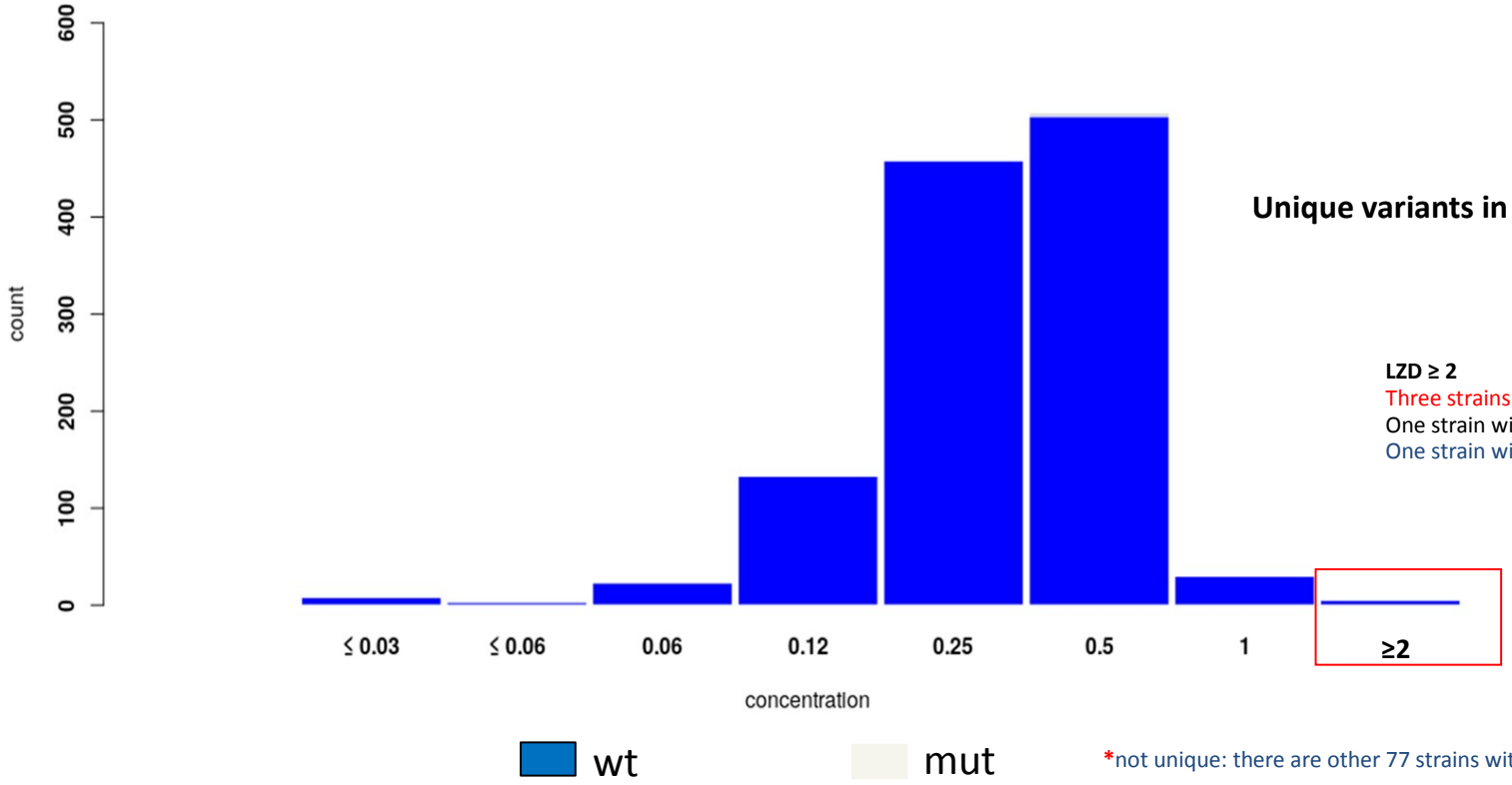
N=1177 strains

Linezolid (LZD)

Genes analyzed for LZD
rplC: Rv0701 (800809-801462)
rrl: Rvnr02 (1473658-1476795)



Unique variants in LZD-R strains:

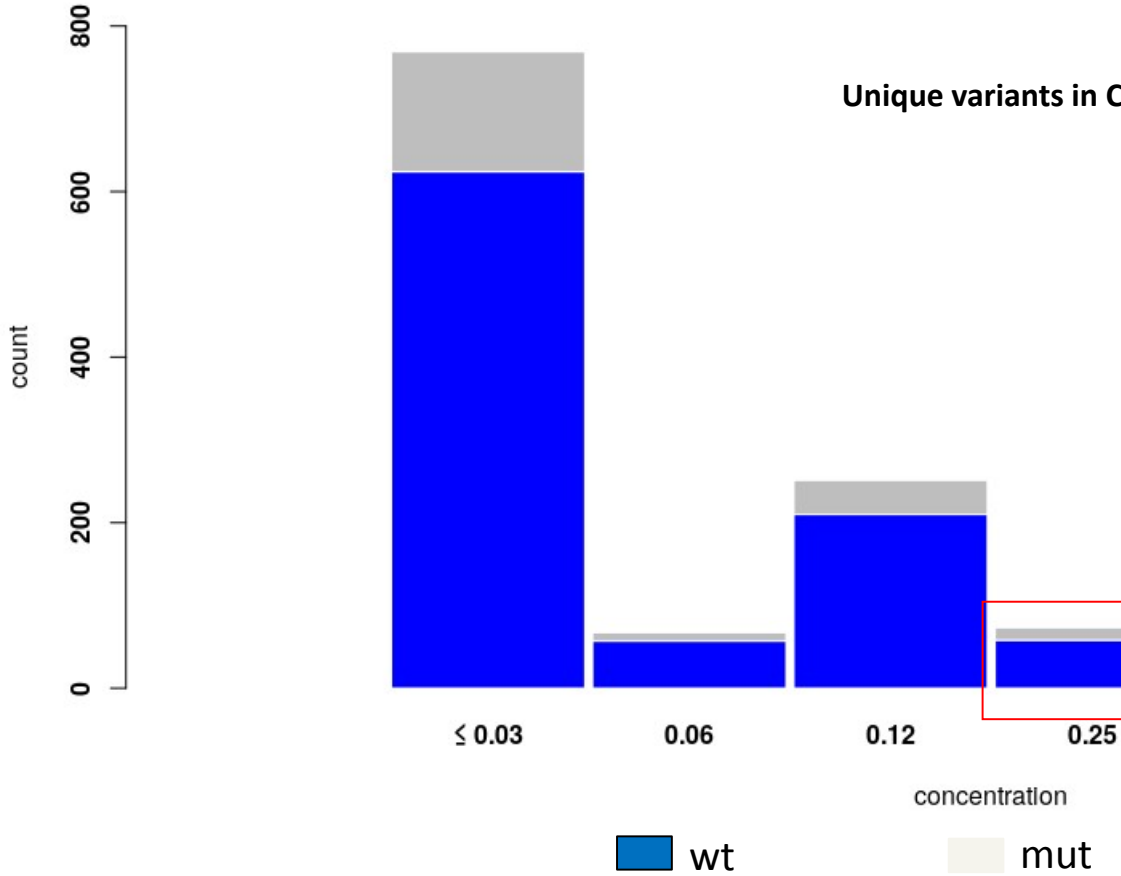
LZD ≥ 2
Three strains with rrl_G2814T mutation
One strain with rrl_C344T mutation*
One strain with MIC ≥ 2 is wt

*not unique: there are other 77 strains with MIC ≤ 1

N=1177 strains

Clofazimine (CFZ)

Genes analyzed for CFZ
Rv0678: -100 bp (778890-779487)
Rv1979c: + 100 bp (2221719-2223264)



Unique variants in CFZ-R strains:

CFZ 0,25
Rv0678_Leu117Arg -> BDQ-MIC of 0.5*
Rv0678_Ile67fs -> BDQ-MIC of 0.25
Eight strains are mutated in Rv1979c
Sixty strains with MIC at 0,25 are wt

CFZ 0,5
Rv0678_Arg38fs -> BDQ-MIC of 0.5*
Rv0678_Leu136Pro -> BDQ-MIC of 0.5*
Rv0678_Gly121Arg -> BDQ-MIC of 0.5*
Rv0678_Leu117Arg -> BDQ-MIC of 0.25
Prom_Rv0678_c.-14G>A mutation & BDQ-MIC of 0.25
Ten strains with MIC at 0,5 are wt

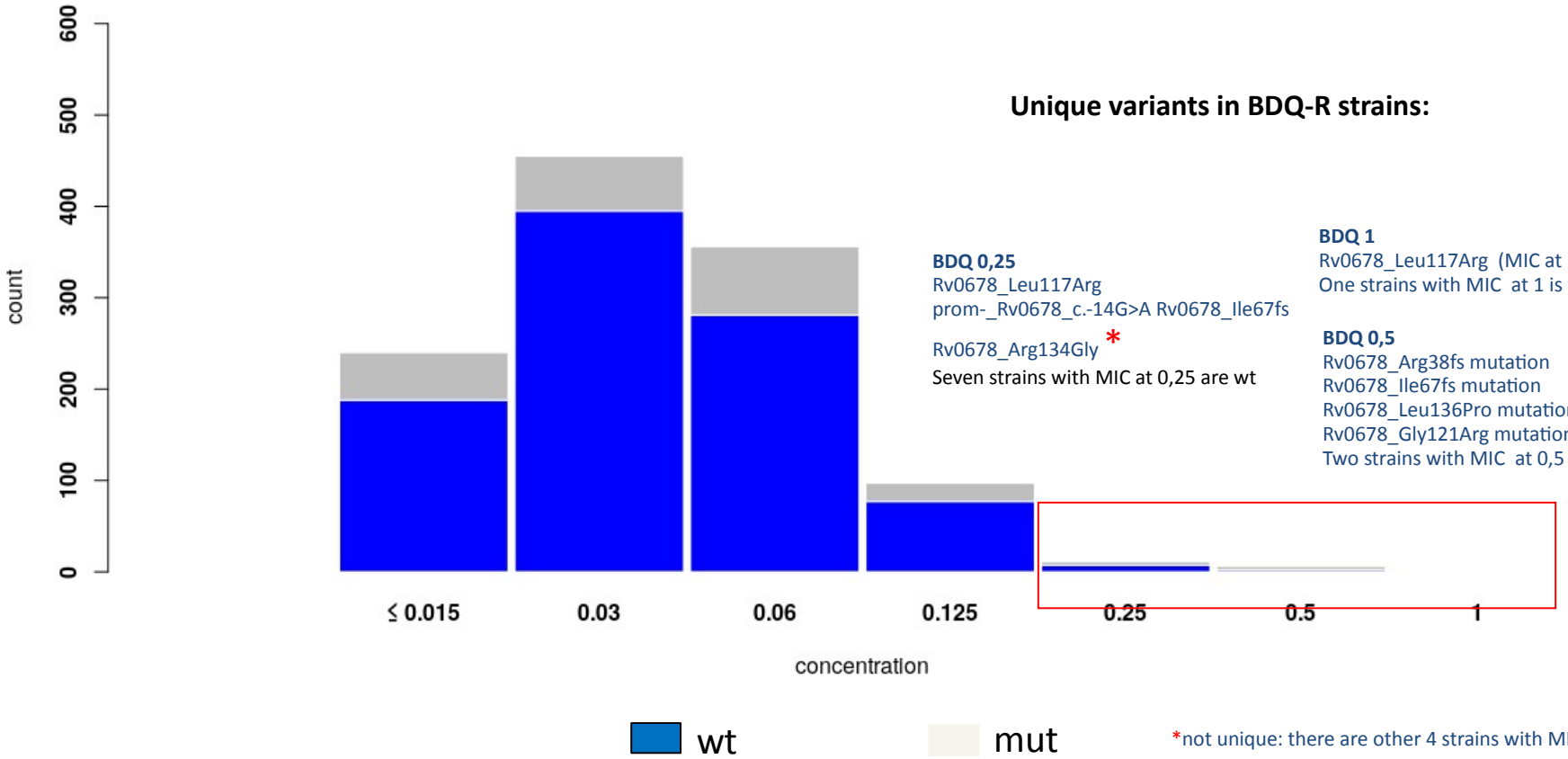
CFZ 1
One strain with MIC at 1 is wt

***In RED** are indicate mutated strains also resistant to BDQ

N=1177 strains

Bedaquiline (BDQ)

Genes analyzed for BDQ
Rv0678: -100 bp (778890-779487)
atpE: Rv1305 (1461045-1461290)
pepQ: Rv2535c: +100 bp (2859300-2860518)



Unique variants in BDQ-R strains:

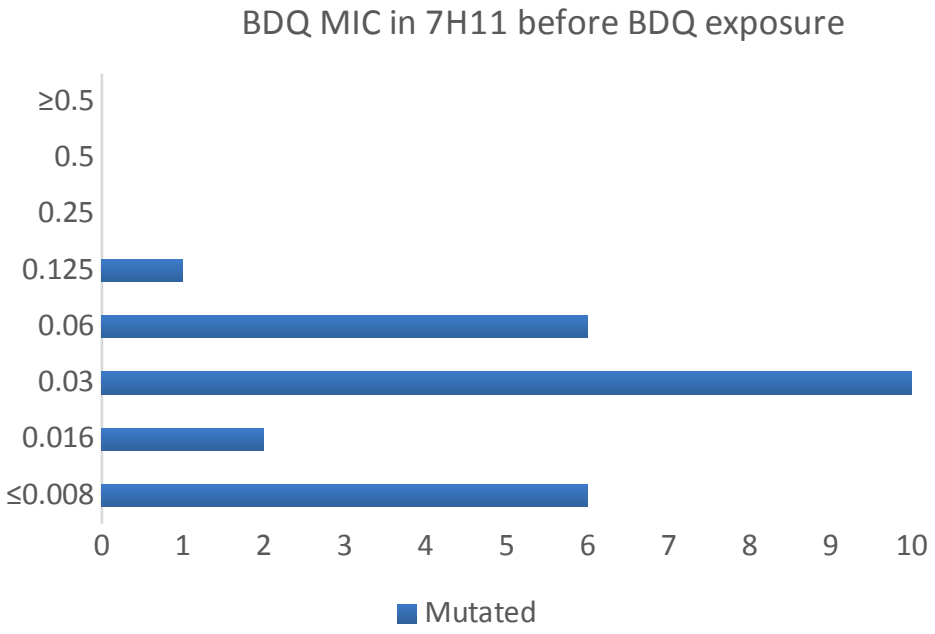
BDQ 0,25
Rv0678_Leu117Arg
prom-_Rv0678_c.-14G>A Rv0678_Ile67fs
Rv0678_Arg134Gly *
Seven strains with MIC at 0,25 are wt

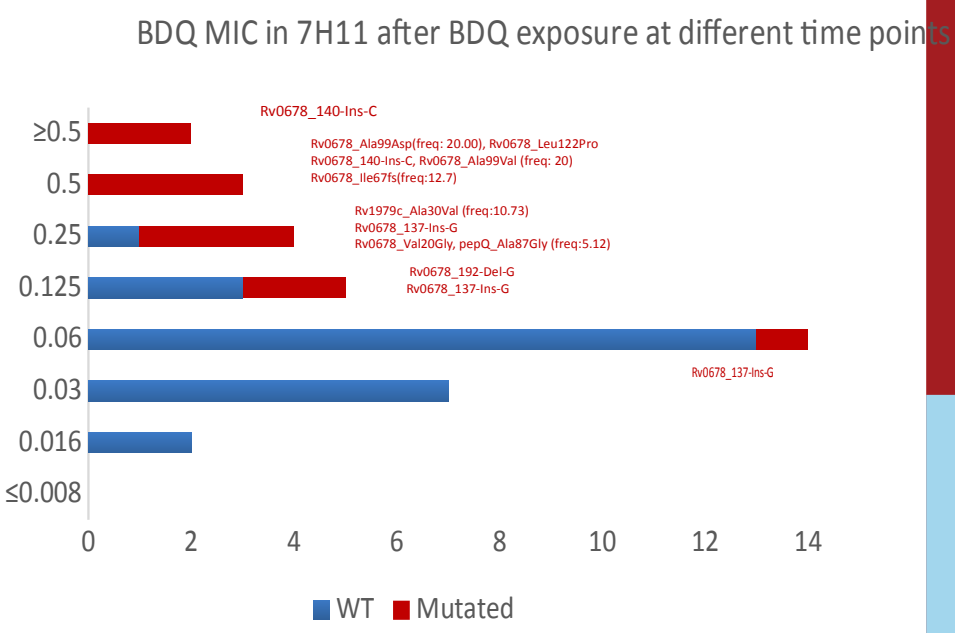
BDQ 1
Rv0678_Leu117Arg (MIC at 1)
One strains with MIC at 1 is wt

BDQ 0,5
Rv0678_Arg38fs mutation
Rv0678_Ile67fs mutation
Rv0678_Leu136Pro mutation
Rv0678_Gly121Arg mutation
Two strains with MIC at 0,5 are wt

*not unique: there are other 4 strains with MIC ≤ 0,12

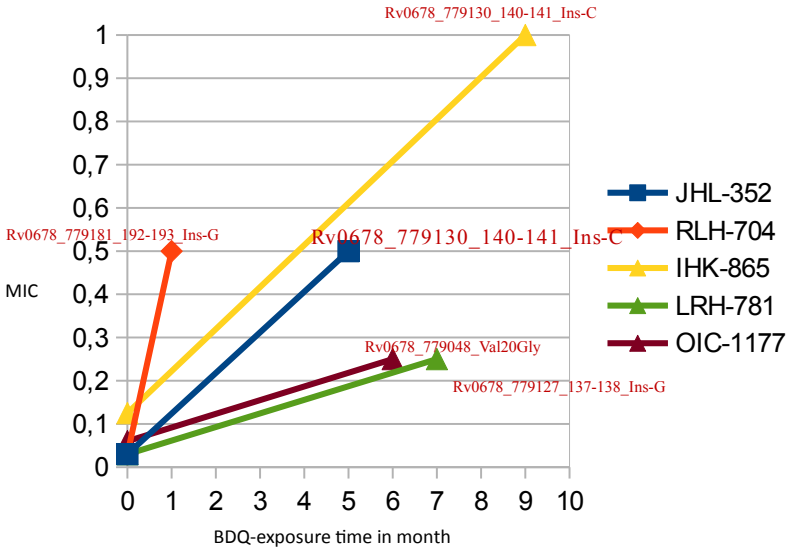
Bedaquiline MIC pre-post exposure



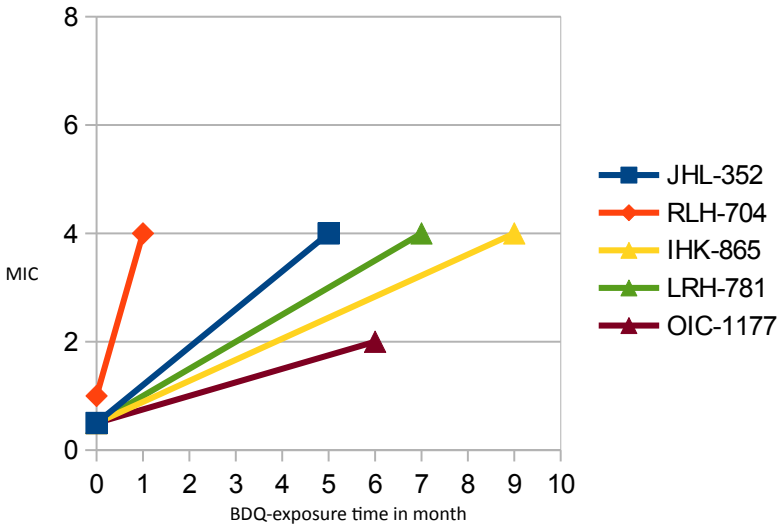


Increase in MIC during treatment

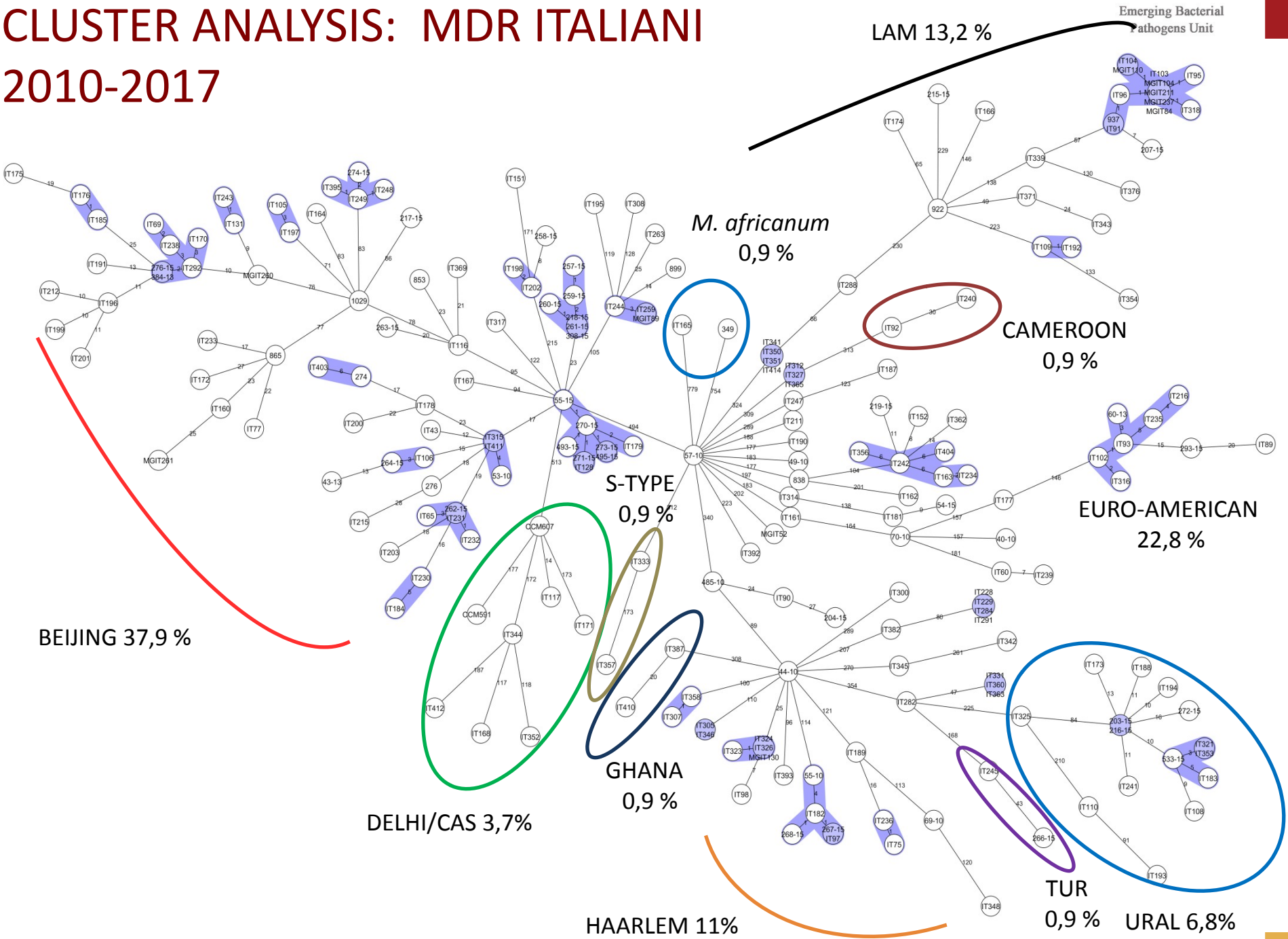
BDQ MIC in 7H11



CFZ MIC in MGIT



CLUSTER ANALYSIS: MDR ITALIANI 2010-2017



EUSeqMyTB

Emerging Bacterial Pathogens Unit

OSPEDALE SAN RAFFAELE

Pilot study on the use of Whole Genome Sequencing for molecular typing and characterization of *M. tuberculosis* for the preparation of genomic surveillance of MDR-TB in the EU/EEA

To generate evidence on the usefulness of WGS for a better understanding of multidrug-resistant (MDR)-TB strain diversity, characterisation of emerging MDR-TB clones, early detection and tracing MDR-TB outbreaks and mapping transmission routes of MDR-TB in Europe.

To set common standards and parameters to be used for WGS analysis across EU

PeerJ

MTBseq: a comprehensive pipeline for whole genome sequence analysis of *Mycobacterium tuberculosis* complex isolates

Thomas Andreas Kohl[1,*], Christian Utpatel[1,*], Viola Schleusener[1], Maria Rosaria De Filippo[2], Patrick Beckert[1,3], Daniela Maria Cirillo[2] and Stefan Niemann[1,3]

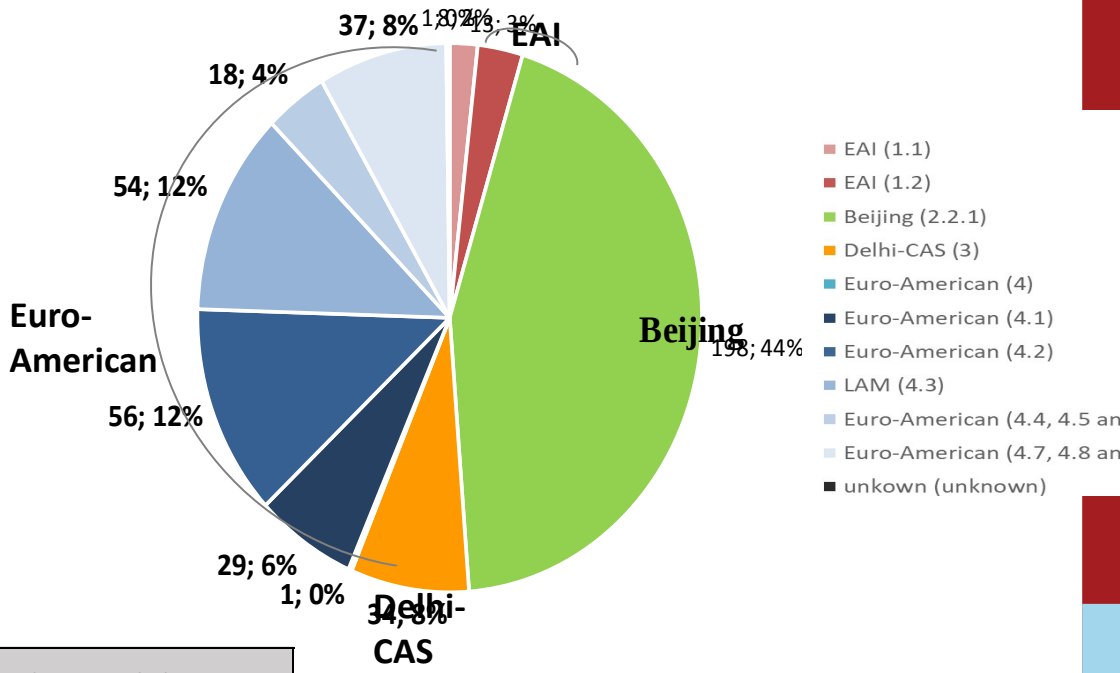
Tagliani E,et al Lancet Infect Dis. 2018 Apr;18(4):377.

In the first 449 isolates from 9 different countries
11 cross-border clusters

Emerging Bacterial Pathogens Unit

OSPEDALE SAN RAFFAELE

Country	No. of strains
Italy	64
Netherlands	15
UK	63
Estonia	30
Belgium	11
Portugal	23
Sweden	20
Germany	169
Lithuania	54
Total	449



SNP-based approach

Clusters involving recent transmission events			
NAME	N. strains	Mean distance between cases	Standard deviation
CL 1	9	1,1	0,9
CL 2	2	1,0	n.a
CL 3	8	1,4	1,3
CL 4	7	2,8	1,5
CL 5	3	3,3	1,5
CL 6	5	5,2	2,6
CL 7	3	2,7	1,2
CL 8	5	4,2	2,0
CL 9	2	3,0	n.a
CL 13	2	2,0	n.a
CL 14	2	2,0	n.a

Clusters involving putative transmission events			
NAME	N. strains	Mean distance between cases	Standard deviation
CL 10	5	6,6	6,8
CL 11	3	6,0	1,7
CL 12	2	7,0	n.a
CL 15	9	10,4	2,5
CL 16	2	7,0	n.a
CL 17	2	12,0	n.a
CL 18	2	12,0	n.a
CL 19	3	8,0	6,9
CL 20	2	12,0	n.a
CL 21	4	8,7	3,8

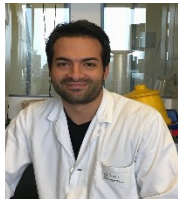
Take home message

- *Abbiamo tecnologie molecolari che permetterebbero un miglioramento del management clinic del paziente, la sorveglianza delle resistenze e supporterebbero le anilisi di trasmissione*
- *Perchè non le usiamo?*
- *L'antibiogramma fenotipico è troppo lungo e costoso e non necessario in molti casi, l'uso delle MICs da informazioni più utili*

Emerging Bacterial Pathogens Unit

PEDALE SAN RAFFAELE

Thank you!



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Timothy EA Peto
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University of Oxford

World TB Day 2019

Join us in Valencia for ESM 2019

Diversification of sputum-based testing and DST

Xpert Ultra
(Cepheid)

Centralized DST
(Abbott, BD, Hain, Roche, Bioneer)

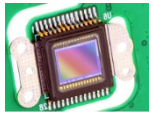
MGIT -
Bedaquiline
Delamanid (BD)

QMAC QDST
(QuantaMatrix)

POC DST
(QuantuMDx, Bioneer,
MicoBiomed, Akonni, …)

TruArray MDRTB /
XDRTB (Akonni)

Q-POC TB/MDR
TB (QuantuMDx)



Hybridisation
(Scanogen)

2017 | 2018 | 2019 | 2020 - 2025

Line probe assays:
- MTBDRplus and sl (Hain Lifescience)
- Lipa MTBDR (Nipro)
- TBmodule (AID)

Liquid culture:
- MGIT (BD)
- TREK Sensitive (Thermofisher)
- Mycolor TR BNP (Salubris)

NAAT:
- Xpert MTB/RIF (Cepheid)
- TB-LAMP (Eiken)
- Mycobacteria RT PCR (CapitalBIo)
- Anyplex MTB/XDR (Seegene)
- Infiniti MDR TB (Autogenomics)
- VereMTB/Rif/Inh (Veredus Laboratorie
- MeltPro MDR (Zeesan Biotech)
- Genedrive TB/Rif (Epistem)
- AccuPower TB/MDR (Bioneer)

First Xpert follower

TrueLab MDR/TB
(Molbio)

→ Enable TEST & TREAT
→ Match the regimen pipeline

Omni Platform (Cepheid)

Expanded DST
(Cepheid, Hain, Bioneer)

End-to-End targeted from sputum

Whole genome Sequencing from sputum

DISCLAIMER: Images & time estimates are to be taken as indicative only.

Adapted from FIND

Thank you