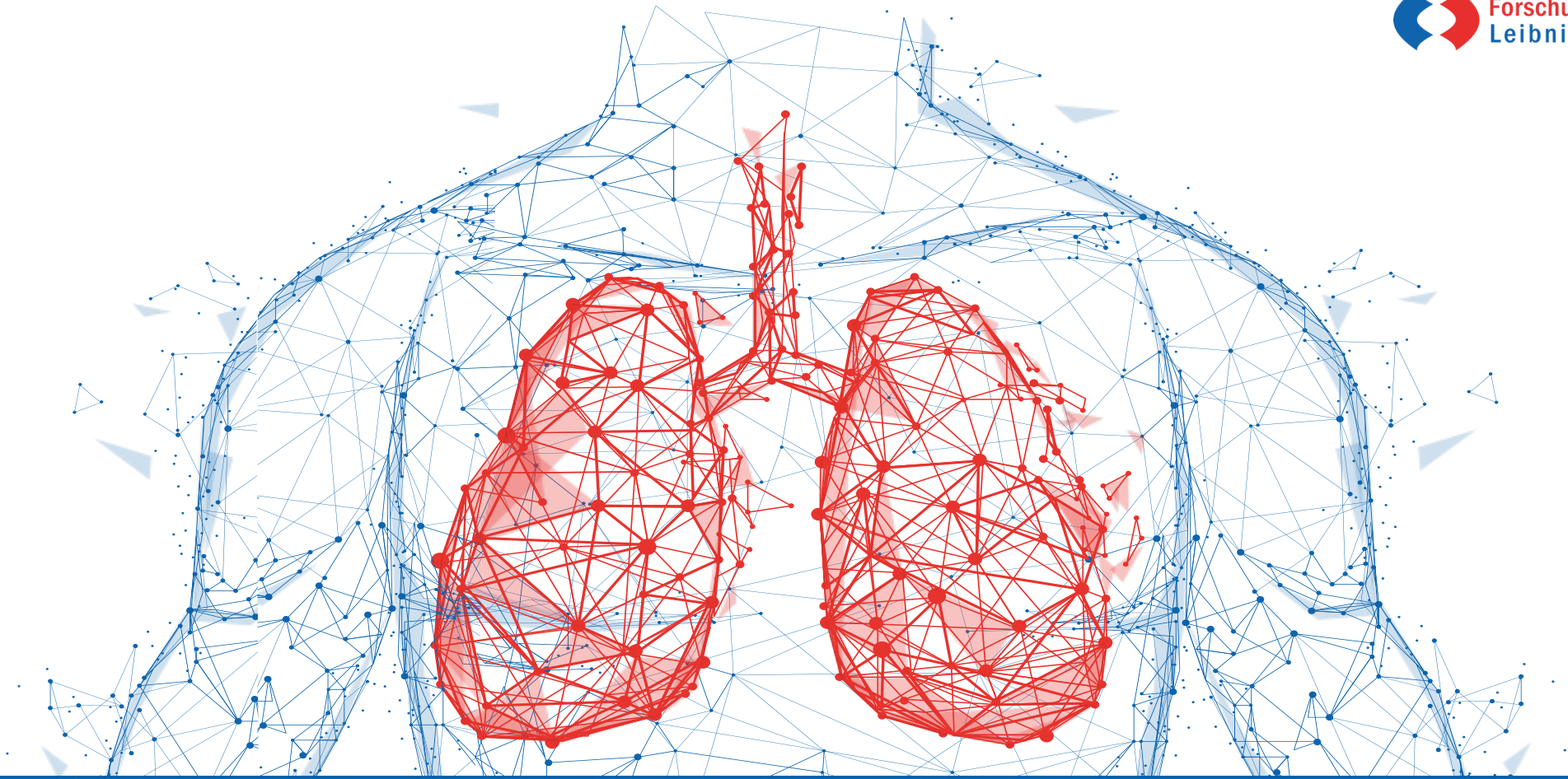




Schnelle Resistenzdetektion

Martin Kuhns

Nationales Referenzzentrum für Mykobakterien

Material: Bronchial-/Trachealsekret

Auraminpräparat

- KEINE säurefesten Stäbchen im Präparat

Direktnachweis mittels NAT

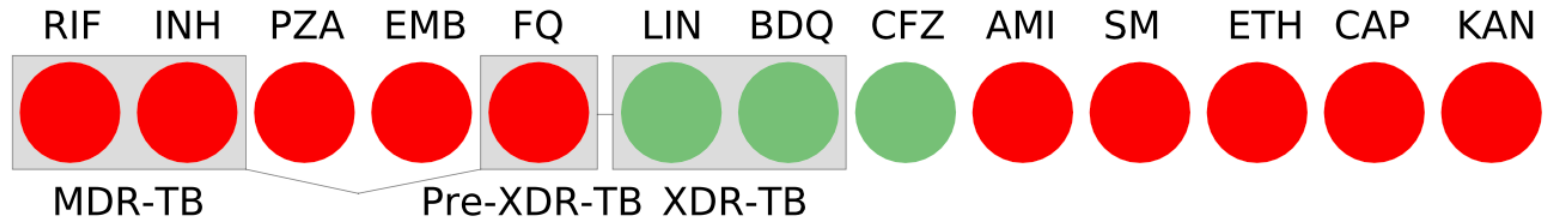
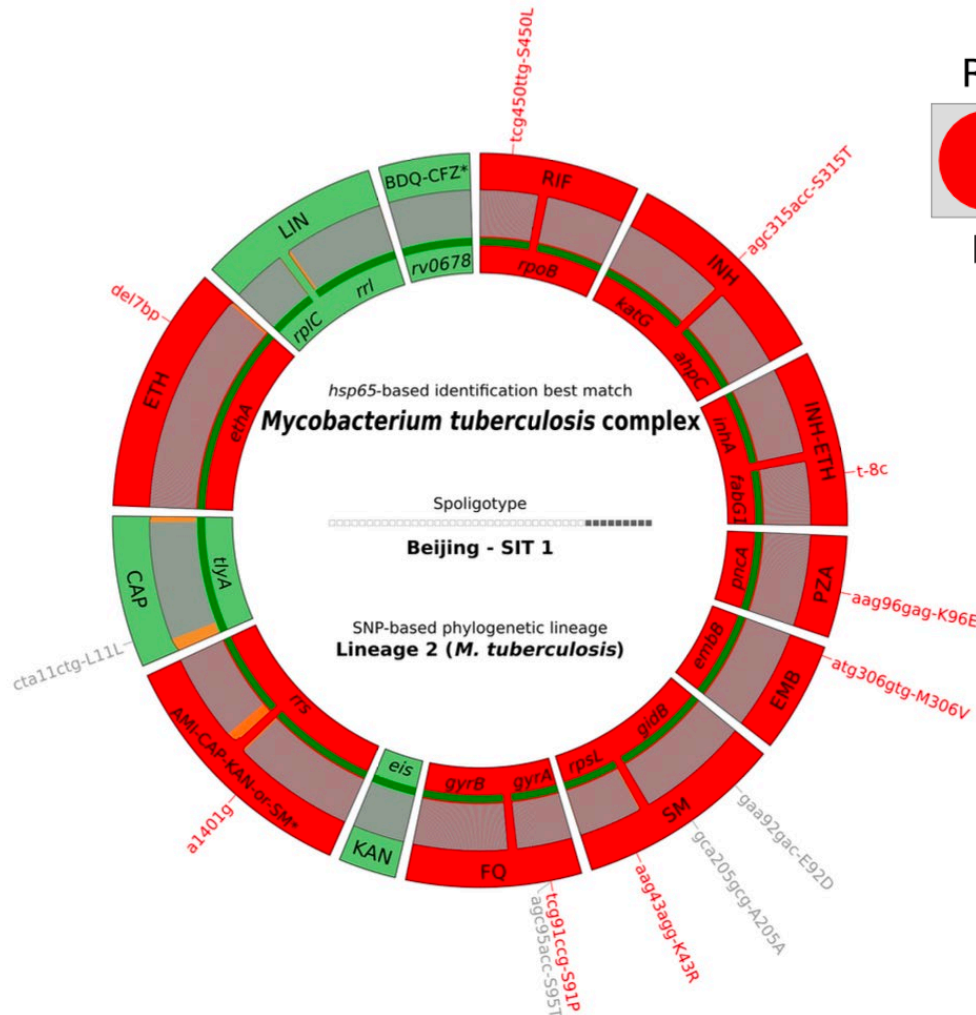
- NACHWEIS von M. tuberculosis-Komplex DNA
- Rifampicin/Rifabutin: rpoB-Gen: Mutation H445N entspr. H526N (RESISTENT)
- Isoniazid: katG-Gen: Mutation S315T1 (RESISTENT)
- Isoniazid/Ethionamid: inhA Promotor: Mutation c-777t entspr. c-15t (RESISTENT)

MDR vs. XDR

Antibiogramm		[1]
Isoniazid	(0,1 mg/l)	R
Rifampicin	(0,5 mg/l)	R
Ethambutol	(5 mg/l)	S
Levofloxacin	(1 mg/l)	S
Moxifloxacin	(0,25 mg/l)	S
Moxifloxacin	(1 mg/l)	S
Bedaquilin	(1,0 mg/l)	S
Linezolid	(1 mg/l)	S
Clofazimin	(1,0 mg/l)	S
Cycloserin	(16 mg/l)	S
Pretomanid	(0,5 mg/l)	S
Amikacin	(1 mg/l)	S
Prothionamid	(2,5 mg/l)	R
Delamanid	(0,06 mg/l)	S

Antibiogramm		[1]
Isoniazid	(0,1 mg/l)	R
Rifampicin	(0,5 mg/l)	R
Ethambutol	(5 mg/l)	R
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Amikacin	(1 mg/l)	R
Prothionamid	(2,5 mg/l)	R
Delamanid	(0,06 mg/l)	R

Schnelle Resistenzprädiktion II (targeted Next Generation Sequencing)



Drug resistance associated variants³

Gene	Genomic position	Codon change	% Variant	Dx-score	AA change	Drug*	Confidence	Resistance level	Reference
<i>embB</i>	4247429	atg306gtg	99.800	245.75	M306V	EMB	Associated with resistance	Resistant	WHO 2021
<i>gyrA</i>	7572	tcg91ccg	99.680	154.75	S91P	LEV,MXF	Associated with resistance	intermediate	WHO 2021
<i>fabG1</i>	1673432	t-8c	99.950	510.00	n/a	ETH,INH	Associated with resistance - Interim	Resistant	WHO 2021
<i>katG</i>	2155168	agc315acc	100.000	92.50	S315T	INH	Associated with resistance	Resistant	WHO 2021
<i>pncA</i>	2288956	aag96gag	99.950	1457.50	K96E	PZA	Associated with resistance	Resistant	WHO 2021
<i>rpoB</i>	761155	tcg450ttg	99.960	661.00	S450L	RIF	Associated with resistance	Resistant	WHO 2021
<i>rpsL</i>	781687	aag43agg	100.000	196.50	K43R	STM	Associated with resistance	Resistant	WHO 2021
<i>rrs</i>	1473246	a1401g	99.890	219.00	n/a	AMI,CAP, KAN	Associated with resistance	Resistant	WHO 2021
<i>ethA</i>	4326289-95	del7bp	93.110	0.00	frameshift	n/a	n/a	Resistant	n/a

Vorzüge vs. Hemmnisse

Vorzüge

- Schnelle Resistenzprädiktion
 - aus Primämaterial
 - 15 Medikamente
 - Innerhalb von ~7 Tagen

Hemmnisse

- IVD-Zulassung (nur Test, nicht Software)
- Abrechnung
- Kosten

Vielen Dank für ihre Aufmerksamkeit.

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Forschungszentrum Borstel



Bundesministerium
für Gesundheit



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AGORA
RESEARCH LETTER



Rapid genomic first- and second-line drug resistance prediction from clinical *Mycobacterium tuberculosis* specimens using Deeplex-MycTB

- 39/50 klinische Proben mit verwertbarem Ergebnis aus tNGS
- 45 Resistenzmutationen; 3 Heteroresistenzen (RMP, INH, FQ) nicht im LPA gefunden; Konkordanz mit Phänotyp 97.4% (RMP), 94.9% (INH)
- 81 Kulturen: Konkordanz von 98% mit WGS

■ Feuerriegel et al., PMID: 32764113