Table 2

Table 2. Characteristic of patients with NTM on granuloma vs patients with other diagnosis on pathology

	NTM/NTM+ Other		Other		Total		P Value
CATEGORY	n	%	n	%	n	%	
Age (years), Mean SD	69.43	10.23	67.66	12.3	67.95	11.99	0.2251
Race							
Caucasian	52	65.8	254	68.1	306	67.70	
African American	2	2.5	35	9.4	37	8.19	.
Asian	18	22.8	27	7.2	45	9.96	*0.0002
Other	4	5.1	29	7.8	33	7.30	.
Not specified	3	3.8	28	7.5	31	6.86	.
Sex							0.9193
Male	33	40.7	172	41.3	205	41.25	
Female	48	59.3	244	58.7	292	58.75	.
Smoking Status							0.1344
Current Smoker	11	13.6	26	6.3	37	7.47	
Former Smoker	37	45.7	194	46.9	231	46.67	.
Non-Smoker	25	30.9	165	39.9	190	38.38	.
Passive Smoker	2	2.5	7	1.7	9	1.82	.
Data Not Available	6	7.4	22	5.3	28	5.66	.
Airborne Isolation							
No	40	49.4	380	92.5	420	85.37	*<0.0001
Yes	41	50.6	31	7.5	72	14.63	.
Necrotizing Granuloma on Pathology							
No	12	14.8	206	50.1	218	44.31	*<0.0001
Yes	69	85.2	205	49.9	274	55.69	.
Past Medical History							
DM	11	13.6	48	11.5	59	11.87	0.6032
HTN	33	40.7	221	53.1	254	51.11	0.0414
CAD	6	7.4	52	12.5	58	11.67	0.1915
Malignancy	16	19.8	57	13.7	73	14.69	0.1593
Autoimmune Disease	7	8.6	28	6.7	35	7.04	0.5385
Other	0	0	5	1.2	5	1.01	0.3213
HIV	0	0	1	0.2	1	0.20	0.6587
History of Prior TB	4	4.9	5	1.2	9	1.81	* 0.021
Underlying Lung Conditions							
Asthma	8	9.9	41	9.9	49	9.86	0.9954
COPD	24	29.6	75	18	99	19.92	*0.0168
Other Malignancy Involving Lung	1	1.2	3	0.7	4	0.80	0.6361
Bronchiectasis	0	0	3	13.214	3	0.60	0.4433

Table 2

Lung Cancer	10	12.3	16	12.662	26	5.23	*0.0017
Interstitial Lung Disease	0	0	10	12.11	10	2.01	0.1586
Pneumonitis	0	0	1	11.558	1	0.20	0.6587
Other Structural Lung Disease	2	2.5	9	11.005	11	2.21	0.8642

Conclusion: Mycobacterial infections made up a significant percentage of resected lung nodules and/or lung masses for malignancy evaluation. NTM were isolated with greater frequency than *M. Tuberculosis* even with NGL on lung pathology. This reflects the changing epidemiology of NTM. The significant proportion of Asians with NTM compared with GL found during a malignancy work up without NTM is interesting and deserves further investigation.

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1653. Estimation of country-specific tuberculosis antibiograms using a wide and deep neural net on a large genomic dataset

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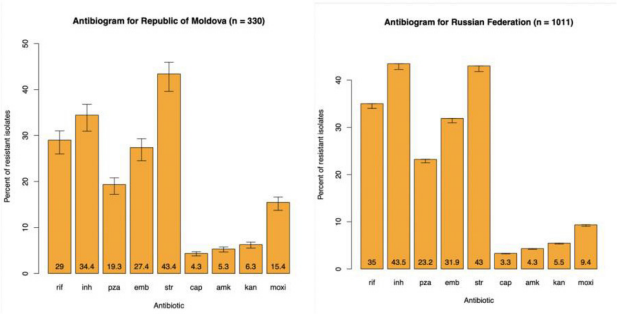
Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Improved estimates of drug resistant tuberculosis (TB) burden are needed to aid control efforts. The World Health Organization (WHO) currently reports estimates for rifampin resistance (RR) or multidrug resistance (MDR) at the national level. Resistance rates to other first-line and second-line agents, e.g. ethambutol, pyrazinamide, and aminoglycosides, are rarely available, even at the country level. Our objective was to generate country and drug specific resistance prevalence estimates (antibiograms) using in silico phenotype prediction and curated public and surveillance Mycobacterium tuberculosis (MTB) genomic data.

Methods. We curated MTB genomes either by sequencing or from published literature and excluded genomes that did not meet our quality criteria (i.e. at least 10X depth in >95% of the genome). A machine learning model previously trained to predict phenotypic resistance in MTB with high accuracy, a wide and deep neural net (WDNN), was used to predict resistance to ten drugs. We corrected for resistance oversampling in genomic data by conditioning on RR and using country specific surveillance MDR/RR rates reported by the WHO.

Results. Of the 49,851 MTB genomes curated, 33,873 isolates met quality criteria. Of these, geographic data was available for 22,838 genomes. Antibiograms were generated for nine first- and second-line drugs for 36 countries. Among countries with at least 100 isolates, a high rate of resistance to fluoroquinolones and second line injectables was seen among isolates from the Republic of Moldova (15.4% [CI = 13.7-16.7%] moxifloxacin resistant, 6.3% [CI = 5.5-6.8%] kanamycin resistant, n = 330) and Russian Federation (9.3% [CI = 9.1-9.4] moxifloxacin resistant, 5.4% [CI = 5.3-5.5%] kanamycin resistant, n = 1011) (Figure 1).

Figure 1: Antibiograms created using genotypic data for isolates from Republic of Moldova (n=330, rifampin-resistance rate correction: 29%, range 26-31% among new tuberculosis cases);and Russian Federation (n=1011, rifampin-resistance rate correction 35%, range 34-35%, among new tuberculosis cases. rif: rifampin, inh: isoniazid, pza: pyrazinamide, emb: ethambutol, str: streptomycin, cap: capreomycin, amk: amikacin, kan: kanamycin, moxi: moxifloxacin



Conclusion: The estimation of antibiotic resistance prevalence in MTB for pyrazinamide, ethambutol and second-line agents can be aided by the use of *in silico* models of drug resistance. A high rate of resistance to second-line drugs precludes large scale roll out of short-course WHO regimens for treatment of MDR-TB for empiric use in certain countries. The use of whole genome sequencing for resistance surveillance can inform policy on optimal national regimen choice for TB treatment.

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1654. Evaluation of a rapid detection method of clarithromycin resistance genes in *Mycobacterium avium* using the Amplification Refractory Mutation System-Loop-Mediated Isothermal Amplification method

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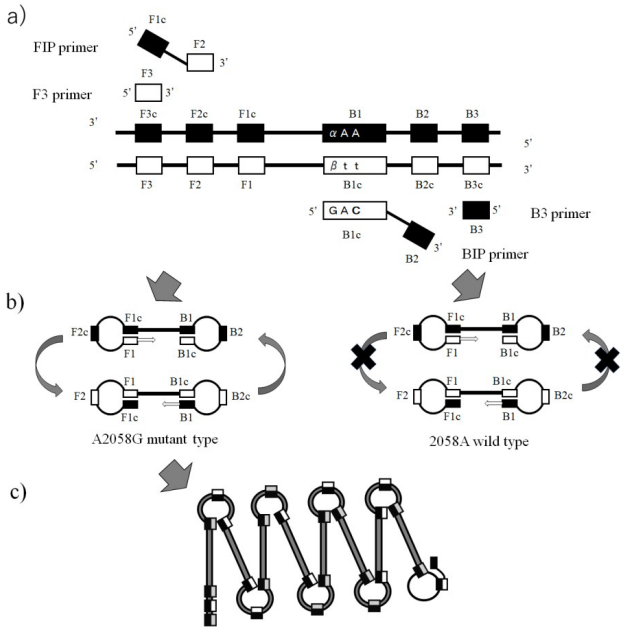
Session: P-72. Tuberculosis and other Mycobacterial Infections

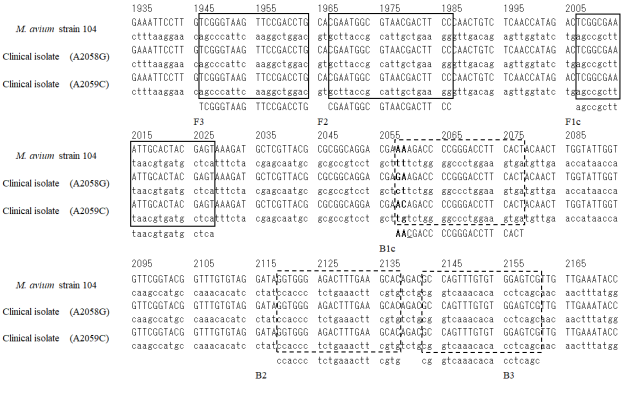
Background. Clarithromycin (CLR) is the key drug in multidrug therapy for *Mycobacterium avium* complex (MAC) diseases and the only drug for which drug susceptibility is correlated with a clinical response in these diseases. In the case of CLR-resistant MAC, a point mutation is present at either position 2058 or 2059 of the peptidyl transferase active center in the domain V region of 23S rRNA at the macrolide binding site. Using conventional investigation, we clarified the correlation between drug susceptibility testing and mutation of drug resistance genes. In this study, we adapted a rapid detection method using the amplification refractory mutation system (ARMS)-loop-mediated isothermal amplification (LAMP) to identify a mutation in the 23S rRNA gene in *M. avium* isolates (Figure 1). Furthermore, we evaluated the usefulness as point-of-care testing (POCT) technology using clinical isolates.

Figure 1. The designs of CLR resistance A2058G mutant-type mismatch primers used for the ARMS-LAMP assay. a) A strand-displacing DNA polymerase extends the DNA from FIP while separating from the DNA chain. The primer F3 binds to its complementary region on the DNA to displace the newly synthesized DNA. An analogous reaction is performed by BIP and B3. α (α = A, wild type; G, A2058G) and β (β = A, wild type; C, A2058G) are indicated by the point mutation at position 2058 of the 23S rRNA gene. The bold area indicates the mismatched base C (cytosine). b) The synthesized DNA self-anneals because of the complementary region at both ends and forms 'dumbbell' structures. c) After repeated rounds, a complementary region on the same chain is amplified.



Methods: Primers for ARMS-LAMP were designed using PrimerExplorerV5 software based on the nucleotide sequence data for 23S rRNA in *M. avium* strain 104 (Figure 2). Using the minimum inhibitory concentration of CLR, drug susceptibility was determined for 18 clinical *M. avium* isolates. Of these, eight CLR-susceptible and 10 CLR-resistant strains were analyzed by sequencing the 23S rRNA gene and ARMS-LAMP.

Figure 2. Alignment of the nucleotide sequences including the domain V region of 23S rRNA at the macrolide binding site. The constructed LAMP primer sets are shown in solid boxes (forward primers, F1-3) and dashed boxes (backward primers, B1-3). The bold area indicates the point mutation at position 2058 or 2059 of the 23S rRNA gene.



Results: Sequence analysis revealed that all eight CLR-sensitive strains tested were wild type, whereas all 10 CLR-resistant strains were mutants. Using ARMS-LAMP, no amplification with the mutant-type mismatch primer sets (MTPS) was observed in the eight wild-type strains, but amplification was observed with MTPS in the 10 mutant strains (Table 1).

Table 1. MICs of CLR and results of ARMS–LAMP using Mycobacterium avium isolates.

Strains	Total number	MIC (μg/mL)	ARMS-LAMP
Reference strain			
Mycobacterium avium 104	1	0.25	-
Clinical isolates			
CLR susceptible strains	8	< 8	-
CLR resistant strains	10	>32	+

CLR, clarithromycin. MIC, minimum inhibitory concentration. +, positive. -, negative. ARMS-LAMP, amplification refractory mutation system -loop-mediated isothermal amplification.

Conclusion: The developed rapid detection method for the CLR resistance gene using ARMS-LAMP can determine drug resistance in a few hours without the need for special equipment. ARMS-LAMP may be a new clinically beneficial POCT technology for examination that is novel and extremely practical.

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1655. Extrapulmonary Tuberculosis in a Large Healthcare System

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. The US has seen a rise in the proportion of patients with extrapulmonary tuberculosis (TB) even though the yearly incidence of new TB cases has been in decline. The purpose of this study was to analyze incidence of extrapulmonary TB at Atrium Health, a large non-profit health system in the Southeastern US.

Methods. Retrospective chart review of 94 adult patients with culture confirmed extrapulmonary TB between 2008-2019. Individuals younger than 18 years were excluded from analysis. The primary objective was to examine incidence of extrapulmonary TB and compare it to that reported in the literature. Secondary objectives included determination of sites of extrapulmonary disease and associated patient characteristics including HIV status, race, ethnicity, and birthplace.

Results. 237 patients were identified as having confirmed TB infection from 2008-2019 in a retrospective analysis within the Atrium Health System. 94 (40%) were found to have extrapulmonary disease; 42 (45%) with concomitant pulmonary disease. The patients were 55% male, 40% African American, 21% Hispanic or Latino, and 51% US-born. Median age was 44 years (range 20-62). The most common sites of extrapulmonary TB were lymphatic (35%), pleural (24%), GI/Peritoneal (12%), CNS (10%), and Bone/Joint (10%). Lymphatic involvement was 40% cervical, 19% intrathoracic, and 16% axillary. 66% of skeletal disease was vertebral. Other sites included GU, pericardial, skin, and disseminated disease (5%). 37% were HIV positive, 18% with unknown HIV status as they were never tested. Information regarding patient's race, ethnicity, and birthplace were unknown for 2 patients. The percentage of extrapulmonary cases were 29% in 2008, 39% in 2012, 38% in 2016, and 49% in 2019.

Conclusion. Lymphatic and pleural involvement were the most common extrapulmonary sites. Of those tested, 37% were HIV positive but there was a significant portion never tested showing a need for increased testing. The proportion of extrapulmonary TB cases since 2008 is higher at 40% compared to the 31% reported in the United States. There has been a rise in the proportion of extrapulmonary TB within our healthcare system and deserves further analysis.

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1656. Factors associated with low TB preventative therapy prescription rates among healthcare workers in rural South Africa

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Session: P-72. Tuberculosis and other Mycobacterial Infections

Background. Despite South Africa's initial successful rollout of tuberculosis preventative therapy (TPT) to reduce tuberculosis (TB) incidence among HIV-infected