

from the same time period with the same genotype were included in the phylogenomic analysis. The genomic variants identified by WGS were used for phylogenomic inference, drug resistance prediction and to determine genomic distances between isolates.

WGS analysis revealed unexpected genomic diversity within the seemingly homogenous IS6110 cluster of *M. tuberculosis* isolates. Despite the IS6110 RFLP based uniformity, at least six non-time dependent sub-clusters and several orphan-isolates were evident from the WGS-based phylogeny and genomic comparisons. Sub-clusters gained drug resistance conferring mutations (beyond MDR) on multiple occasions and *M. tuberculosis* isolates from surrounding suburbs were observed throughout the phylogeny.

IS6110 RFLP typing underestimated the complexity of this 23-year outbreak. This study suggests that there is continuous circulation and reintroduction of this *M. tuberculosis* cluster in the community setting. Even with the advent of the WGS-era, confirming direct epidemiological links or outbreak directionality remains a challenge in high TB burden, low-income settings.

6.13

doi: 10.15789/2220-7619-2018-4-6.13

A 15-YEAR SPATIOTEMPORAL ANALYSIS OF MYCOBACTERIUM TUBERCULOSIS LINEAGES 1 AND 2 IN CHIANG RAI, THAILAND

A. Disratthakit¹, P. Palittapongarnpim^{2,3}, P. Ajawatanawong², N. Smittipat³, S. Mahasirimongkol¹, R. Miyahara⁴, H. Yanai^{5,6}, N. Yamada⁷, S. Nedsuwan⁸, W. Imasanguan⁸, P. Kantipong⁸, B. Chaiyasirinroje⁵, S. Bupachat⁵, P. Ananpradit⁵, W. Ruengchai², T. Juthayothin³, J. Phelan⁹, J. Parkhill¹⁰, T.G. Clark⁹, M.L. Hibberd⁹, K. Tokunaga⁴

¹Department of Medical Sciences, Ministry of Public Health, Thailand; ²Department of Microbiology, Faculty of Science, Mahidol University, Thailand; ³National Centre for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Thailand; ⁴Department of Human Genetics, Graduate School of Medicine, the University of Tokyo, Japan; ⁵TB-HIV Research Foundation, Thailand; ⁶Fukujuji Hospital, Japan Antituberculosis Association (JATA), Japan; ⁷Research Institute of Tuberculosis, JATA, Japan; ⁸Chiangrai Prachanukroh Hospital, Ministry of Public Health, Thailand; ⁹London School of Hygiene and Tropical Medicine, United Kingdom; ¹⁰Wellcome Trust Sanger Institute, Hinxton, United Kingdom

Chiang Rai is the northernmost province of Thailand with high burden of tuberculosis (TB) and high TB death rate. Chiang Rai consists of various ethnic groups in three different geographic areas including (1) the bordering area in the northern and northeastern, (2) the central area, and (3) the outlying districts in the southeastern, southern and southwestern.

We aimed to assess the spatial and temporal distribution of *Mycobacterium tuberculosis* (MTB) lineages in the three different areas over 15 years.

Whole genome sequence (WGS) data was used to classify the genotypes of 1497 MTB using lineage-specific single nucleotide polymorphisms (SNPs). The spatiotemporal distribution of MTB lineage was analyzed in the three different areas during early 2000s (2002–2006), late 2000s (2007–2011) and 2010s (2014–2018). Stoddart and Taylor's index (G) was calculated to determine genotypic diversity of MTB lineage in the different settings.

In 2000s, lineage 2 (East Asian) was a highly predominant genotype (45%) in Chiang Rai followed by lineage 1 (Indo-oceanic) (41%). In 2010s, lineage 1 became the most dominant genotype (51%) replacing lineage 2 (35%).

The overall change in predominant lineage from lineage 2 to lineage 1 was caused by a dramatic increase proportion of lineage 1 in the central area (from 44 to 53%) and in the outlying districts (from 39 to 59%). In the bordering area, a combined impact of increasing distribution of lineage 1 (from 32 to 40%) and other lineages (from 18 to 24%) was an additional cause of changing predominant lineage. The Stoddart and Taylor's analysis of genotypic diversity showed that the central area had the highest diversity of MTB lineage (G = 4.14±0.46) followed by the bordering area (G = 3.67±0.76) and the outlying districts (G = 3.63±0.62).

Our study combining genotypic and space-time analysis has revealed a dynamic population changes in MTB lineage over 15-year period in Chiang Rai. Further studies on social determinants and patient's demographic data in the different geographic areas have the potential to provide effective TB control in the different setting.

6.14

doi: 10.15789/2220-7619-2018-4-6.14

MOLECULAR-GENETIC METHODS OF DETECTION OF TUBERCULOSIS AND ITS DRUG RESISTANCE IN ARKHANGELSK REGION IN 2017

P.I. Eliseev¹, I.V. Tarasova², A.O. Mariandyshv¹

¹Northern State Medical University, Arkhangelsk, Russia;

²Arkhangelsk Regional Antituberculosis Dispensary, Arkhangelsk, Russia

Burden of tuberculosis (TB) is decreasing in Arkhangelsk region in northwestern Russia with incidence declining from 45.9/100 000 in 2012 to 21.6/100 000 in 2017 in civil society (excluding penitentiary society). Introduction of molecular-genetic tests of detection of TB and its drug resistance (DR), including multidrug-resistant (MDR) and extensively drug resistant (XDR) TB, is one of the key components of regional TB program. It plays an important role in improvement of diagnostics and management of TB patients in the region.

The objective was to evaluate performance of molecular-genetic tests used for detection of TB and its DR among patients with TB registered in civil society in Arkhangelsk region in 2017.

Line probe assay (LPA) (Hain Lifescience, Germany) and GeneXpert MTB/RIF (Cepheid, USA) were used for detection of *M. tuberculosis* (MTB) and its DR alongside conventional sputum smear microscopy (SM) and culture. All patients were initially tested with SM followed by LPA (Genotype MTBDR_{plus}) if result of SM was positive or GeneXpert if result was negative using the same sample. In case of DR to isoniazid and/or rifampicin, Genotype MTBDR_s was performed to detect additional DR to fluoroquinolones and injectables, including XDR. In cases suggestive of nontuberculous mycobacteria (NTM), SM or culture positive with negative results of LPA or GeneXpert for MTB, identification was performed using Genotype Mycobacterium CM/AS.

Total of 214 "new cases" and 28 "relapses" of TB were registered in Arkhangelsk region in 2017. MTB was detected in 160 (74.8%) out of 214 "new cases" and all of them were tested for DR using molecular-genetic tests. 53 patients (31.1%) had MDR-TB, among them 3 patients had additional DR to injectables and 2 patients had XDR-TB. Among 28 "relapses" MTB was detected in 24 (85.7%) patients. 13 patients (54.2%) had MDR-TB, among them in 1 patient additional DR to injectables and in 2 patients to fluoroquinolones was detected. NTM associated disease was diagnosed in 4 patients (2 — *M. avium*, 1 — *M. goodii*, 1 — *M. interjectum*).