

**ANALISIS *WHOLE GENOME SEQUENCING*:  
FILOGENI *MYCOBACTERIUM TUBERCULOSIS*, POLA RESISTENSI  
OBAT ANTI-TUBERKULOSIS, DAN MUTASI GEN**



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ANALISIS *WHOLE GENOME SEQUENCING*:  
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ABSTRAK

Indonesia berada pada peringkat kedua angka kejadian TB dan peringkat ketiga angka kematian TB di dunia. Dibutuhkan pendalaman epidemiologi molekuler untuk memahami kasus TB, salah satunya melalui *Whole Genome Sequencing* (WGS). Penelitian ini bertujuan untuk mengetahui filogeni *Mycobacterium tuberculosis* (Mtb), pola resistensi Obat Anti-Tuberkulosis (OAT), dan mutasi gen melalui analisis WGS.

Penelitian ini adalah penelitian deskriptif bidang bioinformatika, menganalisis 18 sampel Mtb yang memiliki hasil *sequencing* dengan metode *Next-Generation Sequencing* dari Laboratorium Mikrobiologi Fakultas Kedokteran Universitas Andalas. *Sequence* setiap sampel diperiksa dengan aplikasi Geneious dengan genom referensi *H37Rv*. Filogeni Mtb diperiksa dengan algoritma RAXML. Mutasi gen terkait resistensi OAT diperiksa dengan *Variations/SNPs Finding*.

Hasil penelitian menunjukkan sampel tergolong ke dalam tiga filogeni, yaitu *Indo-Oceanic* (8 sampel), *East-Asian/Beijing* (5 sampel), dan *Euro-American* (5 sampel), yang dikelompokkan menjadi dua kelompok besar *Beijing* dan *Non-Beijing*. Diperoleh mutasi terkait resistensi OAT pada gen *katG* S315T (3 sampel), *rpoB* S450L (4 sampel), dan *nudC* Q237P (8 sampel). Sebanyak 60% sampel dari kelompok filogeni *Beijing* menunjukkan resistensi MDR/RR-TB, sedangkan hanya 7,69% sampel dari kelompok *Non-Beijing* yang menunjukkan resistensi MDR/RR-TB. Rerata jumlah mutasi dan jumlah gen bermutasi pada kelompok filogeni *Indo-Oceanic*, *East-Asian/Beijing*, *Euro-American*, secara berturut-turut adalah  $5.563,63 \pm 412,28$  dan  $265,00 \pm 7,54$ ;  $4.633,80 \pm 745,42$  dan  $168,60 \pm 4,83$ ;  $3.665,60 \pm 408,48$  dan  $106,40 \pm 14,84$ .

Pada penelitian ini, kami dapat menyimpulkan bahwa filogeni *Indo-Oceanic* ditemukan sebagai filogeni dengan jumlah sampel terbanyak. Mutasi utama terkait resistensi OAT terdapat pada gen *katG*, *rpoB*, dan *nudC*. Persentase MDR/RR-TB yang lebih besar terdapat pada kelompok filogeni *Beijing* dibandingkan *Non-Beijing*.

**Kata kunci:** *Whole Genome Sequencing*, *Mycobacterium tuberculosis*, filogeni, mutasi gen

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ANALYSIS OF WHOLE GENOME SEQUENCING:  
PHYLOGENY OF MYCOBACTERIUM TUBERCULOSIS,  
THE RESISTANCE PATTERN OF ANTI-TUBERCULOSIS DRUGS  
AND GENE MUTATIONS

ABSTRACT

Indonesia ranks second in the incidence of TB and ranks third in the TB mortality rate in the world. Molecular epidemiology is needed to understand TB cases, one of which is through the Whole Genome Sequencing (WGS). This study aimed to determine the relationship of Mycobacterium tuberculosis phylogeny with Anti-Tuberculosis drugs resistance patterns and gene mutations through the analysis of Whole Genome Sequencing.

This was a descriptive study in bioinformatics, analyzing 18 samples of Mtb which had sequenced results with the Next-Generation Sequencing (NGS) method from the Microbiology Laboratory of the Medical Faculty of Universitas Andalas. The sequences of each samples were examined using Geneious with H37Rv as the reference genome. The phylogeny of Mtb was determined using the RAxML algorithm. Mutations in genes related to Anti-TB drug resistance were examined through the Variations/SNPs Finding.

The results showed the sample belonged to three phylogenies, namely Indo-Oceanic (8 samples), East-Asian/Beijing (5 samples), and Euro-American (5 samples), which were grouped into two major Beijing and Non-Beijing groups. Gene mutations related to drug resistance in the katG S315T (3 samples), S450L rpoB (4 samples), and nudC Q237P (8 samples) were obtained. As many as 60% of the samples from the Beijing phylogeny group showed MDR/RR-TB resistance, while only 7.69% of the samples from the Non-Beijing group showed MDR/RR-TB resistance. The mean of the number of mutations and the number of mutated genes in the Indo-Oceanic, East-Asian/Beijing, Euro-American phylogeny groups, respectively were  $5,563.63 \pm 412.28$  and  $265.00 \pm 7.54$ ;  $4,633.80 \pm 745.42$  and  $168.60 \pm 4.83$ ;  $3,665.60 \pm 408.48$  and  $106.40 \pm 14.84$ .

In this study, we can conclude that Indo-Oceanic was found as the phylogeny with the highest number of samples. The main mutations associated with drug resistance were in the katG, rpoB, and nudC genes. The greater MDR/RR-TB percentage was found in the Beijing phylogeny group compared to Non-Beijing.

**Keyword:** Whole Genome Sequencing, Mycobacterium tuberculosis, phylogeny, gene mutation