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Nucleotide Sequences and Mutations in *Katg* Gene in Clinical Isolates of *Mycobacterium tuberculosis* Isolates Resistant to Isoniazid in Papua-Indonesia

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Abstract: Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. Resistance to RIF is caused by mutations in the *rpoB* gene encoding the β subunit of RNA polymerase, with the highest frequency at codon 526 and 531. While Isoniazid is a *prodrug*, must be activated by the enzyme catalase-peroxidase encoded by the gene katG of M. tuberculosis, this gene mutation resulting in INH resistant. The purpose of this research is to obtain information on the cause of the genotype level resistance to INH in clinical isolates of the MDR-TB. Stages of research conducted here is Polymerase Chain Reaction (PCR) allele-specific multiplex *katG*, agarose gel electrophoresis, determining the nucleotide sequence, and *in silico* analysis. Results PCR and agarose gel electrophoresis for all isolates showed two DNA bands measuring 0.4 kb and 0.3 kb. Homology analysis to compare the results of sequencing electropherogram 0.4 kb fragment *katG* gene of the isolates with the same fragment of *M. tuberculosis* strain H37Rv standard. PyMOL modeling results describe the position of each amino acid as a result of mutations in the DNA level in the three-dimensional structure of protein molecules M. tuberculosis catalase-peroxidase. Analysis of data obtained showed that the mutation G946T three isolates located at codon 316, GGC into TGC, resulting in the amino acid glycine is mutated to cysteine. Simulation of the spatial structure of catalase peroxidase with PyMOL program showed 316 amino acid residues near the active site binding INH. Catalase-peroxidase simulation with PyMOL program showed 290 amino acid residues located in the N terminus loop area and relatively far from the active site, the effect of these mutations and their relationship in the nature of resistance to INH unknown. Other isolates G795A mutated nucleotide located at codon 265, TTG into TTA, but did not cause amino acid changes that can be ascertained that the mutation is not the cause of the nature of the resistance. While isolate mutated at codon 315, which has been proven as a cause of INH resistance. The results of this study are expected to provide new information on the position of the mutation in the gene katG of M. tuberculosis that is resistant to INH therefore G946T mutation (Gly316Cys) and C896T (Ala290Val) to isolate not been previously reported.
Keywords : Isoniazid, *katG* gene, MDR-TB, PCR, Isolate Papua.

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