

RESEARCH ARTICLE

Distribution of rs1801279 and rs1799930 Polymorphisms in *NAT2* Gene among Population in Kupang, Nusa Tenggara Timur, Indonesia

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Abstract

BACKGROUND: N-acetyltransferase-2 (*NAT2*) enzyme, encoded by *NAT2* gene, plays a key role in metabolism of anti-tuberculosis (TB) drug isoniazid. Polymorphisms in *NAT2* gene may result in different responses to TB therapy. Since TB prevalence in the eastern part of Indonesia is high, the aim of this study is to explore the distribution of *NAT2* gene polymorphisms among population from Kupang, Nusa Tenggara Timur.

METHODS: A total of 234 respondents were included from Kupang in 2012. Polymorphisms of *NAT2* gene were examined using mass screening platform and the genotypes distribution were presented in percentage. To confirm *NAT2* gene polymorphisms, polymerase chain reaction (PCR)-sequencing was performed in a subset of population.

RESULTS: The polymorphisms of *NAT2* gene showed that the distribution of rs1801279 for GG genotype was 100%; whereas the genotype distribution of rs1799930 for GG, GA and AA was 57%, 35.1% and 7.9%, respectively. In a subset of individuals (n13), acetylator status was well determined by PCR-sequencing, resulting in individual with wild type fast acetylator (*NAT2**4; n4), intermediate (*NAT2**4/*5 or *NAT2**4/*6 or *NAT2**4/*7; n7) and poor acetylators (*NAT2**6/*6 or *NAT2**7/*7; n2).

CONCLUSION: The amino acid change in rs1799930 result in intermediate and poor acetylator status in Kupang population. This may lead to suboptimal response of TB therapy. Assessing acetylator status before TB therapy is important and may serve as personalized INH therapy.

KEYWORDS: *NAT2* gene, polymorphism, acetylator status, Kupang

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Introduction

N-acetyltransferase-2 (*NAT2*) enzyme plays a key role in metabolism of a variety of drugs, including anti-tuberculosis (TB) drug isoniazid (INH). (1) This enzyme is encoded by polymorphic *NAT2* gene which is located at chromosome 8, identified as 8p22. There are at least 7 single nucleotide polymorphisms (SNPs) in *NAT2* gene, *i.e.*, nucleotide (nt) change of 191G>A at rs1801279, nt282C>T at rs1041983,

nt341T>C at rs1801280, nt481C>T at rs1799929, nt590G>A at rs1799930, nt803A>G at rs1208, and nt857G>A at rs1799931, respectively. The distribution of these SNPs is listed in the International data base and has been reported differently in various ethnicities around the globe. (2)

Of note, the nucleotide change does not always result in a change of coded amino acid, for example at the position nt282C>T and nt481C>T; whereas in other positions amino acid do change, for example at the position nt590G>A there is a change from arginine (Arg) to glutamine (Gln)