

Association between *NUDT15* polymorphisms and thiopurine-
induced leukopenia in pediatric acute lymphoblastic leukemia
patients: a systematized review

by

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Abstract

Background: Thiopurines are commonly used to treat acute lymphoblastic leukemia (ALL). A recent genome-wide association study shows the variants of *NUDT15*, an enzyme involved in thiopurine metabolism, are associated with thiopurine-induced leukopenia. This study aims to organize the literature on the relationship between the occurrence of leukopenia and the *NUDT15* gene polymorphism in pediatric ALL patients and to examine the differences in associations due to ethnicity.

Methods: A literature search was performed for *NUDT15* as a keyword using PubMed. Eligible studies included the following inclusion criteria: 1) participants are pediatric ALL patients, 2) ethnic group of the participants is clear, 3) analyzing the association between *NUDT15* gene polymorphism and leukopenia. Minor allele frequency (MAF) of rs116855232 was calculated based on each result of the study.

Results: A total of 16 studies were included. All of them were reported from Asian countries, except Ethiopia and Sweden. All studies in Asian countries showed a strong positive association between *NUDT15* variants and thiopurine-induced leukopenia, while a Swedish report indicated no relationship between *NUDT15* variants and leukopenia. MAF of rs116855232 in Asia is between 0.050 and 0.168, while MAF in Non-Asian countries is relatively low, and there is no allele in studies in Ethiopia. The difference in the association between Asians and non-Asians seems to be from the difference in MAF.

Conclusion: The present study summarized the association between thiopurine-induced leukemia and *NUDT15* gene polymorphisms in pediatric ALL patients. It is hoped that the

distribution of *NUDT15* polymorphisms will be clarified and that treatment guidelines will be established for each ethnicity.

Keywords: ALL, NUDT15, thiopurine-induced leukopenia