



Trends in **Molecular Biology** • Special issue

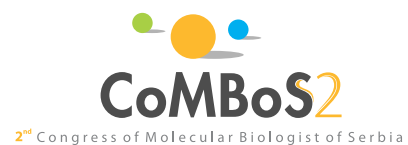
Abstract Book

CoMBoS²

2nd Congress of Molecular Biologist of Serbia

Belgrade • 2023

ISBN-978-86-82679-15-8



**CoMBoS2 – the Second Congress of Molecular Biologists of Serbia,
Abstract Book – Trends in Molecular Biology, Special issue**

06-08 October 2023, Belgrade, Serbia

Online Edition

<https://www.imgge.bg.ac.rs/lat/o-nama/kapacitet-i-oprema/istrazivacka-delatnost>

<https://indico.bio.bg.ac.rs/e/CoMBoS2>

IMPRESSUM

PUBLISHER:

**Institute of Molecular Genetics and Genetic Engineering (IMGGE),
University of Belgrade**

FOR THE PUBLISHER:

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Institute of Molecular Genetics and Genetic Engineering (IMGGE),

University of Belgrade

Belgrade, 2023

ISBN 978-86-7078-173-3

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Belgrade • 2023

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***NUDT15* AS POTENTIAL MARKER FOR PHARMACOGENETIC-GUIDED 6-MERCAPTOPURINE THERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA IN SERBIA**

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Introduction: The *NUDT15* is new pharmacogene of importance for 6-mercaptopurine therapy, given to children with acute lymphoblastic leukemia (ALL). The association of side effects in children with variants in *NUDT15* are well established in Asian populations, yet the relevance of this pharmacogene in European populations remains largely unexplored. The aim of this study was to identify pharmacogenetic variants in coding and neighbouring regions of *NUDT15* gene and analyse if the expression levels of *NUDT15* can predict the occurrence of side effects of 6-mercaptopurine during the maintenance therapy in children with ALL of Serbian origin.

Methods: The genotyping of coding and neighbouring regions of *NUDT15* gene was performed using PCR and Sanger sequencing based technology in 48 children with ALL. *NUDT15* expression was analyzed in mononuclear cells of 24 ALL patients at diagnosis and 6 healthy controls by qRT-PCR, and association with surrogate markers was assessed using adequate statistical methodology.

Results: The genotypig revealed the presence of 5 variants in *NUDT15* (*NUDT15*(NM_018283.4):c.36A>C, *NUDT15*(NM_018283.4):c.158+117C>T, *NUDT15*(NM_018283.4):c.158+174G>A, *NUDT15*(NM_018283.4):c.159-91G>A, *NUDT15*(NM_018283.4):c.*7G>A), none of them with effects on the expression or the function of *NUDT15* protein. There was no statistically significant association between the expression of *NUDT15* at diagnosis and the surrogate markers of side effects (number of episodes of leukopenia (p=0.821), number of weeks without therapy (p=0.507), number of weeks with lower dose (p=0.434), average doses (p=0.374)) of 6-mercaptopurine during the maintenance therapy.

Conclusion: Presently, *NUDT15* cannot be used as a pharmacogene in predicting the toxicity of 6-mercaptopurine therapy in children with ALL in Serbia.

Key words: *NUDT15*; 6-mercaptopurine; pharmacogene; acute lymphoblastic leukemia

Acknowledgements: This work was supported by grant No. 451-03-47/2023-01/200042 Ministry of Education, Science and Technological Development, Republic of Serbia.