

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36607

Title: Influence of NUDT15 Variants on Hematological Pictures of Patients with Inflammatory Bowel Disease Treated with Thiopurines

Reviewer's code: 00070280

Reviewer's country: Sri Lanka

Science editor: Yuan Qi

Date sent for review: 2017-10-17

Date reviewed: 2017-10-27

Review time: 10 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

This is a very good article on an important subject. However, there are a few concerns that need to be addressed first. Title should read Influence of NUDT15 Variants on Hematological Pictures of Asian Patients with Inflammatory Bowel Disease Treated with Thiopurines. Did the authors do folate and B12 levels on these patients? The authors should discuss if it is necessary to do TPMT testing on Asian patients as the mutant prevalence is low.

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Name of journal: World Journal of Gastroenterology

Manuscript NO: 36607

Title: Influence of NUDT15 Variants on Hematological Pictures of Patients with Inflammatory Bowel Disease Treated with Thiopurines

Reviewer's code: 01467363

Reviewer's country: Slovenia

Science editor: Yuan Qi

Date sent for review: 2017-10-17

Date reviewed: 2017-10-27

Review time: 10 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
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		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Title and running title: define the content of the manuscript.
Key words: 5, suitable for the content of the manuscript. Abstract: 346 words, structured, is appropriate.

Introduction: 255 words, listed are basic facts about thiopurine treatment in patients with inflammatory bowel disease and most common adverse effects of this drug (leukopenia, acute pancreatitis, liver dysfunction...)

Method: 529 words, methodology (including patients selection, DNA extraction, Sanger Sequencing, SNP Genotyping) and statistical analysis are clearly explained. In the chapter are included 2 tables (demographic data/treatment and primer sequence for Sanger sequencing analysis) ?

Results: 515 words, included is 1 table (Genotypes of NUDT15 and TPMT) with 4

figures, a/b (1 - absolute count/decrease of WBC: comparing groups A,B,C vs D, 2 - absolute count of WBC: comparing groups A,B,C vs D with and without PSL, 3 - absolute count and decrease ration of WBC in three groups: comparing groups A + B vs C vs D without PSL, 4 - comparing MCV in groups A+B+C vs D and increase ratio of MCV in groups A+B+C vs D).

Discussion: 446 words, short, the authors discuss different genotypes of NUDT15 which were confirmed in several projects in the last years («1000 genomes» project, »5000 exomes« project and »Exome Aggregation Consortium«). They highlight the fact that new genotypes of NUDT15 in patients with ALL (acute lymphoblastic leukemia) were reported. In IBD already several reports on analysis of NUDT15 were reported, however, the authors studied only one SNP site (c.415C>T, encoding p.Arg139Cys) in exon 3. The authors of the presented study analyzed in 96 Asian patients three additional genetic variants including c.36_37insGGAGTC (encoding p.Val18_Val19insGlyVal) and c.52G>A (encoding p.Val18Ile) in exon 1 and c.416G>A (encoding p.Arg139His) in exon 3. According to the results obtained, they conclude that using next generation sequencer, it will become easier to provide the information of NUDT15 SNPs and that further investigation is necessary to see the correlation of NUDT15 SNPs - thiopurine metabolites - induction of side effects. The discussion is modest, the reader is somewhat disappointed.

Conclusions: last paragraph, short, 47 words in the chapter dicussion.

References: 21, relevant, contemporary, influential journals in the field of gastroenterology/hematology/inflammatory bowel disease/genetics (NEJM, Nature Genetics, Pharmacogenomics,...) in the timeframe 1989 (Annals of internal medicine) - 2017 (Journal of gastroenterology and hepatology).

Conflict of interest: none.

Ethics of the study: the study was reviewed and approved by the Institutional Review Board of Yamanashi Prefectural Central Hospital and informed consent was obtained by all the patients.

Funding: this work was not supported by any foundation. There are a few typographical errors in the manuscript.

The article is interesting, however, necessary are maior corrections.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 36607

Title: Influence of NUDT15 Variants on Hematological Pictures of Patients with Inflammatory Bowel Disease Treated with Thiopurines

Reviewer's code: 00038617

Reviewer's country: Japan

Science editor: Yuan Qi

Date sent for review: 2017-10-17

Date reviewed: 2017-11-02

Review time: 16 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
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COMMENTS TO AUTHORS

In this study, the authors evaluated 4 SNPs of both NUDT15 exon 1 and exon 3 on inflammatory bowel disease treated with thiopurines and correlated with biochemical parameters. They examined the change of WBC, MCV, Plt, Hb, CRP, Amy, Alb, AST and ESR with or without prednisolone. Their results were almost reasonable and informative. However, there are several issues to be revised. It is necessary for the authors to modify this manuscript for publication. (1) The authors analyzed WBC count with and without prednisolone. In the cases with prednisolone, WBC count was not significantly lower at other than 8 and 10 weeks. The authors should discuss the reason. (2) Did the side effect of the hair loss appear in this study? (3) Did the side effect of the agranulocytosis appear in this study? (4) The authors should describe the limitations of this study in discussion section.