

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 31928

Title: Thiopurine Use is Associated with Reduced B and Natural Killer Cells in IBD

Reviewer's code: 00049331

Reviewer's country: Turkey

Science editor: Ze-Mao Gong

Date sent for review: 2016-12-17 20:12

Date reviewed: 2016-12-18 14:58

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" 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 checked="" 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 checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In this study authors aimed to determine if and how thiopurine use is associated with depletion of specific lymphocyte populations. Authors demonstrated that a relative lymphopenia associated with thiopurine use is attributable to decreased NK and B cells, rather than T cell depletion. This is a good study and it gives us a well information in terms of thiopurine mechanism. However studies design should be checked and rearranged. Aim of study should be pay attributed and placed either in abstract and in introduction. Result informations that comes from this study should be removed in introduction. After correction, this study is acceptable.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 31928

Title: Thiopurine Use is Associated with Reduced B and Natural Killer Cells in IBD

Reviewer's code: 01022086

Reviewer's country: Belgium

Science editor: Ze-Mao Gong

Date sent for review: 2016-12-17 20:12

Date reviewed: 2016-12-21 18:48

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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The authors have performed a flow cytometric analysis to quantify the immune subsets in healthy controls versus IBD patients, either treated or not with thiopurines. The data show that T cells are not affected, whereas B and NK cells are reduced upon thiopurine use. This is a descriptive manuscript; it does not give any mechanistic insight in the effect of thiopurines on B and NK cells. Major: 1) Fig. 1A should include the results of healthy controls. In analogy with all the other figures, it would also be best to show the 'No Thiopurine' before the 'Thiopurine' results. Fig. 1C should also show the Treg cell numbers per ml. These Treg cell numbers will probably not be different between healthy controls and IBD patients. 2) The NK cell data should be completed by also showing CD56bright and CD56dim cell numbers, in combination with CD16 expression. 3) It is surprising and unexpected that less than 20% of the CD4+FOXP3+Helios+ cells express CD25 (supplemental fig 2). Minor: 1) Grammatical errors: ? Abstract, line 4: 'their ability control IBD at lower doses': include 'to' (control) ? p. 9, line 1: 'our data suggest': suggests ? Fig. 1 legend: 'Thiopurine use associated with lymphopenia': include 'is' (associated) ? Supplemental figure 1 legend: 'TCRva24/ja18 TCRva7.2': replace 'a' with 'α' 2) It should be indicated how lymphocytes, monocytes and



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granulocytes were defined. 3) Which are the CD3- CD19- cells that are not CD56+ NK cells?

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 31928

Title: Thiopurine Use is Associated with Reduced B and Natural Killer Cells in IBD

Reviewer's code: 00055041

Reviewer's country: Italy

Science editor: Ze-Mao Gong

Date sent for review: 2016-12-17 20:12

Date reviewed: 2016-12-21 19:11

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

The paper is interesting. The manuscript would benefit from inclusion of introducing/bridging sentences between the individual parts of the "Results" that explain the logical order and rationale for the experiments. In the Discussion, the Authors should highlight the possible clinical significance of their findings.