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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36449
Title: Childhood-onset inflammatory bowel diseases associated with mutation of Wiskott–Aldrich syndrome protein gene
Reviewer's code: 02440884
Reviewer's country: Germany
Science editor: Ze-Mao Gong
Date sent for review: 2017-11-01
Date reviewed: 2017-11-01
Review time: 7 Hours

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

COMMENTS TO AUTHORS

The authors investigate the frequency of mutations in Wiskott Aldrich in patients suffering from IBD. The mutation WAS c.1378C>T, p.Pro460Ser is associated with a higher frequency of malignomas, which is important for the long-term follow-up. Comments 1. The study is hampered by the small number of patients included. This point should be more addressed.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36449
Title: Childhood-onset inflammatory bowel diseases associated with mutation of Wiskott–Aldrich syndrome protein gene
Reviewer's code: 03478404
Reviewer's country: Romania
Science editor: Ze-Mao Gong
Date sent for review: 2017-11-01
Date reviewed: 2017-11-03
Review time: 2 Days

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

COMMENTS TO AUTHORS

In this paper, the authors performed screening for Wiskott–Aldrich syndrome and chronic granulomatous disease in people with pediatric-onset of IBD. Without any doubt, the manuscript is nicely written, the structure is appropriate and references are adequate. Particularly, I've noticed attention to details. However: 1. The number of children (18) is too small and this is a real major drawback. 2. Only 3 children were found with WAS gene c.1378 C>T p.Pro460Ser mutation and they did not show neither thrombocytopenia nor increased susceptibility to infection. According to the presented data, they did not have any peculiarities, including clinical aspects, endoscopy and therapy. 3. No child was found with CGD (probably, again, due to the small number of included children). 4. The authors wrote "Despite the lack of typical clinical manifestations of WAS, low expression of WASP could be associated with the

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pathogenesis of a subtype of IBD patients." How do we know that this could be associated with IBD pathogenesis? 5. What is the importance of these findings for our practice? Do they change our therapeutic and/or monitoring approach? The authors mentioned :" WAS is known to be associated with an increased risk of malignancies including lymphoma, as well as autoimmune diseases. Therefore, in any long-term follow-up, the analysis of WASP expression in children with IBD should be considered even if major symptoms of WAS are absent." But any IBD could be associated with autoimmune diseases and malignancies, including lymphoma. Therefore, we screen IBD patients for these conditions anyway. This is part (or should be part) of our daily basis practice. 6. The authors wrote "IBD is caused by both genetic and environmental factors". Please do not forget about epigenetics, microbiota and immune responses. 7. I thought a control group would have been very important. And, indeed, later in their paper, the authors wrote "Blood samples were also collected from healthy young adults as a control." What were the findings in this control group? I did not find any mention. This could be of crucial importance. 8. The authors wrote: "Screening for underlying immunodeficiencies may contribute to improving patient management and outcome." I fully agree with this statement, but this is not the conclusion after analysing the patients mentioned in this study. 9. Legend of the endoscopic images should be re-written to correspond to the pictures.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36449
Title: Childhood-onset inflammatory bowel diseases associated with mutation of Wiskott–Aldrich syndrome protein gene
Reviewer's code: 02446483
Reviewer's country: Canada
Science editor: Ze-Mao Gong
Date sent for review: 2017-11-01
Date reviewed: 2017-11-04
Review time: 3 Days

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

COMMENTS TO AUTHORS

Inflammatory bowel disease (IBD) is chronic in nature with a relapsing course and both comprises Crohn's disease (CD) and ulcerative colitis (UC) as well as indeterminate colitis with overlapping features of CD and UC. Although affecting people of the 2nd and 3rd decades of life, IBD may also affect infants and children. IBD is suggested to result from disturbed interactions between the immune system and commensal bacteria of the gut, but theories may involve the environmental factors as well. The immune theory is substantially backed by murine models showing that colitis does not develop in gnotobiotic mice, but emerges on reconstitution of the gut flora. The authors present interesting data with involvement of the Wiskott -Aldrich gene. The manuscript is very interesting, although terminology needs to be addressed (there are some inconsistencies) and in the discussion the role of the environment and epigenomics should be

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emphasized.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36449
Title: Childhood-onset inflammatory bowel diseases associated with mutation of Wiskott–Aldrich syndrome protein gene
Reviewer's code: 01557050
Reviewer's country: Japan
Science editor: Ze-Mao Gong
Date sent for review: 2017-11-01
Date reviewed: 2017-11-12
Review time: 10 Days

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

COMMENTS TO AUTHORS

1) General comments Dr. Ohya and Yanagimachi, et al. investigated 'Childhood-onset inflammatory bowel diseases associated with mutation of Wiskott-Aldrich syndrome protein gene. The article is informative and well-presented. The reviewer has some comments. Comments 1) Please describe in Discussion whether WAS mutation would be the prediction for cutaneous complication with TNF-α or not.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36449
Title: Childhood-onset inflammatory bowel diseases associated with mutation of Wiskott–Aldrich syndrome protein gene
Reviewer's code: 01047558
Reviewer's country: Tunisia
Science editor: Ze-Mao Gong
Date sent for review: 2017-11-01
Date reviewed: 2017-11-13
Review time: 12 Days

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

COMMENTS TO AUTHORS

The manuscript "Childhood-onset inflammatory bowel diseases associated with mutation of Wiskott–Aldrich syndrome protein gene" found WAS c.1378C>T, p.Pro460Ser mutation in three IBD patients. This result doesn't allow us to say that this mutation could be a risk factor for IBD development. The population is very small, the mutation exists in IBD patients without WAS syndrome and in WAS patients without IBD. I do not see the interest of looking for this mutation in IBD patients neither for the diagnosis nor for the prognosis.