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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 37423
Title: Phenotypic and genotypic characterization of inflammatory bowel disease in children under six years of age in China
Reviewer's code: 03254778
Reviewer's country: United States
Science editor: Xue-Jiao Wang
Date sent for review: 2017-12-12
Date reviewed: 2018-01-05
Review time: 23 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] 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

A very good descriptive study of VEOIBD in children in China. There are some phrases which read awkwardly in English which require mild polishing. Figure 1 was missing in the manuscript file.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 37423
Title: Phenotypic and genotypic characterization of inflammatory bowel disease in children under six years of age in China
Reviewer's code: 02529422
Reviewer's country: Japan
Science editor: Xue-Jiao Wang
Date sent for review: 2018-01-12
Date reviewed: 2018-01-16
Review time: 3 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[Y] 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

Major comment: The authors reported a largest cohort study of monogenic diseases among VEOIBD patients diagnosed by next generation sequence. In this manuscript, the authors suggest the difference in diagnosed monogenic diseases among China and Western countries. However, there are several issues to consider before accepting the manuscript: 1: The authors are discussing on details of each diseases using about 2 pages (Line 334- Line 388), but none of these findings written here are novel. The reviewer suggest the most important result in this manuscript is that IL10 deficiency and XIAP were predominant in this cohort, in contrast to Western countries, as the authors mentioned in line 394. Emphasizing this section with more detailed citation, and summarizing description of each diseases are recommended (e.g. writing details of all the diseases in just one paragraph). 2: There are 2 limitations in this study, however the

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authors mentioned very little about this. The authors did not perform any functional studies for novel mutations, therefore there might be false positive for these patients, except for patients showed elevated serum IL10 levels. The authors have not described criteria for selecting patients to take genetic testing. Not testing every patients might lower detection rate of monogenic IBD among the cohort. Furthermore, the authors have used 2 methods of NGS but how these tests were chosen are not mentioned. The authors should clarify this, and the reviewer suggest using one paragraph for explaining limitations in this manuscript. 3: The authors have written that VEO-IBD patients accounted for 34.9% of pediatric patients. However these values were not written in result section. Moreover, since how many percentages of all pediatric IBD patients in your province (or community) are referred to your hospital is unclear, it is difficult to directly compare this percentage with other cohort studies. The reviewer suggest write whole number of pediatric IBD patients and percentage of VEOIBD at the beginning of result, and delete from discussion. Minor comment: 1) Figure 1 is missing. 2) Write every gene names in Italic letters. 3) Use term 'monogenic' but not 'monogenitic'. 4) What is assembly of chromosome locations described in this manuscript? GRCh37 or CRCh38? 5) Add SNP IDs (start with rs….) for all known variants (Table 5). 6) Results are divided to 7 sections, and only some of these titles are written in Bold letters. Check the manuscript again and use bold letters for all the titles, or use numbers instead. 7) Some results are written in percentages, however considering sample size, all percentage values should be rounded off to the first decimal (e.g. 57.41% to 57.4%). 8) Line 121: The term 'incidence' is used as number of patients who developed disease per 'general population' in a year. When the overall cohort only includes patients, this term cannot be used. In this manuscript, the reviewer suggest using the term 'the percentage of VEO-IBD among all pediatric IBD patients'. 9) Line 125: Add non-abbreviated term for 'M' (months). 10) Line 129: Add non-abbreviated term for BMI. 11) Line 145: The term 'Time to diagnosis' is unclear. Did you want to mean 'Median time from the disease onset to diagnosis'? 12) Line 164: Add non-abbreviated term for CVID (and note mistyped as CIVD here). 13) Line 173: 'Level of IL10' should be 'serum IL10 level' 14) Line187: Is 'amino acid formula' same as 'elemental formula'? 15) Line 207: In the sentence 'His older sister had one mutation', did you want to say the sister is a hereditary carrier? 16) Line 213: Please add adult normal range of serum IL10. 17) Line 236: CD4/CD >CD4/CD8? 18) Line 243: Add non-abbreviated term for Ig (Immunoglobulin) 19) Line 244: Add non-abbreviated term for IVIG 20) Line 251: Please specify that these mutations are on TNFRSF13B gene. 21) Line274: Most of the studies on clinical features of VEOIBD include monogenic IBD patients. Do the authors suggest monogenic IBD patients should be excluded from these studies, or just want to say the geographic, ethnic difference among studies affected difference in genetic background and therefore caused conflicting results? If the latter is

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what the authors want to say, describe in that way. 22) Line 281: Please change description of citation as follows; Kammermeirer et al. 23) Line 291; When using the term 'prevalence' solely, usually it means 'number of patients per general population. If you want to describe 'the percentage of VEOIBD among all the pediatric IBD patients in your hospital', the reviewer suggest writing in that way. Alternatively you can write 'prevalence of VEOIBD among all the pediatric IBD patients in our hospital'. 24) Line 310: The reviewer suggest the author should mention if clinical findings mentioned in the citation are similar to this cohort or not. 25) Line 332: The sentence 'However…' should be deleted from here and write a paragraph about limitation of this manuscript instead. 26) Line 334-388: Nothing novel is written here. The reviewer suggest this section should be completely deleted or summarized. 27) Line 400: The importance of this manuscript and what is new in this manuscript should be described in conclusion.