

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 13228

Title: PNPLA3 I148M variant in nonalcoholic fatty liver disease: demographic and ethnic characteristics and the role of the variant in nonalcoholic fatty liver fibrosis

Reviewer code: 00742517

Science editor: Yuan Qi

Date sent for review: 2014-08-13 20:16

Date reviewed: 2014-08-27 19:47

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The manuscript of 'PNPLA3 I148M variant in nonalcoholic fatty liver disease: demographic and ethnic characteristics and the role of the variant in nonalcoholic fatty liver fibrosis' reviews the role of the PNPLA3 SNP (I148M) in nonalcoholic fatty liver disease (NAFLD), and discusses the underlying mechanisms. As a result, association between PNPLA3 I148M and NAFLD is uncovered in adult and pediatric population. This association may be affected by gender and ethnicity, but not by the presence of metabolic syndrome. Moreover, PNPLA3 I148M variant takes an important place in the NAFLD-related liver fibrosis, probably by stimulating the Hh signaling pathway and then activating hepatic stellate cells (HSCs). These achievements may add a new level to our knowledge about the genetic background of NAFLD, thereby provide us with novel access to the clinical therapy. Major comments 1.This manuscript clearly summarizes a well-known PNPLA3 variant, I148M, that underlies NAFLD. Regretfully, association of PNPLA3 I148M and the spectrum of NAFLD (simple steatosis, nonalcoholic liver disease, nonalcoholic steatohepatitis), and also its histopathological mechanisms, have already been reviewed previously. Thus there maybe limited origination in this manuscript. 2.According to the manuscript, 'we explore the role of the PNPLA3 I148M in the development of nonalcoholic fatty liver fibrosis and hypothesize the underlying mechanisms by speculating a pro-fibrogenic network' (page 2), and 'we speculate a pro-fibrogenic network that the PNPLA3 I148M variant may promote the development of fibrogenesis by activating the Hh signaling



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pathway' (page 3). However, reviewer does not be able to find the composition of pro-fibrogenic network. Exact definition of this network is then suggested. Minor comments 1. The effect of PNPLA3 I148M on NAFLD, and NAFLD-related liver fibrosis, has been uncovered in patients with different age, gender, and ethics. Taken into account of the multiple clinical trials, table rather than text seems to be a best solution to display these findings.

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ESPS manuscript NO: 13228

Title: PNPLA3 I148M variant in nonalcoholic fatty liver disease: demographic and ethnic characteristics and the role of the variant in nonalcoholic fatty liver fibrosis

Reviewer code: 02890067

Science editor: Yuan Qi

Date sent for review: 2014-08-13 20:16

Date reviewed: 2014-08-26 13:41

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is an interesting paper which may improve our knowledge in the fields. The subject matter is suitable for the intended audience and it fits the journal scope. Article is mostly clearly written, but Title is suggestive of the article's content. Article is appropriately organized and the headings are indicative of content I suggest to accept this paper in the present form

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ESPS manuscript NO: 13228

Title: PNPLA3 I148M variant in nonalcoholic fatty liver disease: demographic and ethnic characteristics and the role of the variant in nonalcoholic fatty liver fibrosis

Reviewer code: 00069262

Science editor: Yuan Qi

Date sent for review: 2014-08-13 20:16

Date reviewed: 2014-08-26 23:06

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

It is a good review on the subject. Usually when it is a paper review the tables and figures help to understand the issue. I suggest making two or three tables bringing together information on the subject, and add one or two more figures.

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ESPS manuscript NO: 13228

Title: PNPLA3 I148M variant in nonalcoholic fatty liver disease: demographic and ethnic characteristics and the role of the variant in nonalcoholic fatty liver fibrosis

Reviewer code: 00069814

Science editor: Yuan Qi

Date sent for review: 2014-08-13 20:16

Date reviewed: 2014-09-05 15:42

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Interesting review. Some more tables and figures will make it easier for the reader to follow. language revision is needed