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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39103

Title: Mouse models for investigating the underlying mechanisms of nonalcoholic hepatitis-derived hepatocellular carcinoma

Reviewer's code: 03646639

Reviewer's country: Japan

Science editor: Ze-Mao Gong

Date sent for review: 2018-04-04

Date reviewed: 2018-04-08

Review time: 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input checked="" type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Takakura K et al summarize the established mouse models which are most representative of metabolic syndrome-associated NASH induced HCC and discuss the underlying hepatic mechanisms of NASH-related tumorigenesis. I suggest that they



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should describe the other metabolic syndrome-associated-HCC models (for example, dietary NAFLD induced HCC C57Bl/6 J mice fed a high fat, high carbohydrate diet developed HCC at week 52).

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ No

BPG Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39103

Title: Mouse models for investigating the underlying mechanisms of nonalcoholic hepatitis-derived hepatocellular carcinoma

Reviewer's code: 02528832

Reviewer's country: Spain

Science editor: Ze-Mao Gong

Date sent for review: 2018-04-04

Date reviewed: 2018-04-09

Review time: 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Authors should either include a list with the abbreviations or define all of them in the text. Minor problems with English language (for instance, page 8 "proceeded" (?) Perhaps preceded?)



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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39103

Title: Mouse models for investigating the underlying mechanisms of nonalcoholic hepatitis-derived hepatocellular carcinoma

Reviewer's code: 02861131

Reviewer's country: Moldova

Science editor: Ze-Mao Gong

Date sent for review: 2018-04-04

Date reviewed: 2018-04-17

Review time: 13 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Manuscript Number: 39103 Manuscript Title: MOUSE MODELS FOR INVESTIGATING THE UNDERLYING MECHANISMS OF NONALCOHOLIC HEPATITIS-DERIVED HEPATOCELLULAR CARCINOMA Comments To Authors

SPECIFIC COMMENTS 1) The original findings of this manuscript – that is review article; the new hypotheses that this study proposed- summarized data about NASH-HCC progression animal models; the hypotheses that were confirmed through experiments in this study – not relevant review article 2) The quality and importance of this manuscript - the authors of this article have been assessed the mouse models for investigating the underlying mechanisms of nonalcoholic hepatitis-derived hepatocellular carcinoma. The importance and significant of the research is high because research on NASH pathogenesis and carcinogenesis is ongoing and till now we do not have clarity in this point; the new findings of this study – the molecular mechanisms underlying progression to hepatocellular carcinoma from nonalcoholic steatohepatitis that have been identified to date using the array of mouse models currently available and popular in the experimental field the new concepts that this study proposes - the author has presented different animal model which confirmed tumorigenic mechanisms of NASH-HCC progression; the new methods that this study proposed - do not propose new methods; the conclusions do not appropriately summarize the data that this study provided; the unique insights that this study presented - mouse models are essential for investigating the underlying mechanisms of NASH-HCC progression; the key problems in this field that this study has solved - the author has presented different animal model which confirmed tumorigenic mechanisms of NASH-HCC progression 3) The limitations of the study and its findings - the considerable demerit of genetic mouse model, however, is the obscurity of the original gene of tumorigenesis for HCC due to lack of genetic manipulation and the inclusion of diabetes and hyperlipidemia in the background. Genetic manipulation in mouse models, such as of the PTEN-KO or ALR-KO, is a useful means by which to clarify the role of a specific gene in the molecular foundation of NASH-HCC progression; although, the sequential progression to HCC in these models has a relatively long duration and HCC occurrence is uncertain; the

future directions of the topic described in this manuscript - the future research targets may move forward towards gaining a more comprehensive NASH-HCC evaluation by using these mouse models; the questions/issues that remain to be solved - it is still questionable whether or not these available mouse models represent the initiating and/or progression processes of bona fide human NASH-HCC; the questions that this study prompts for the authors to do next - further inquiries are expected by researchers upon selecting an appropriate NASH mouse model according to the specific mechanisms and/or therapeutic targets of interest; this publication impact basic science and/or clinical practice - help to understand mechanism of NASH-HCC progression

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