

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 38083

Title: Antiviral effects of hepatitis B virus S gene-specific anti-gene locked nucleic acid in transgenic mice

Reviewer's code: 02447091

Reviewer's country: Japan

Science editor: Xue-Jiao Wang

Date sent for review: 2018-02-09

Date reviewed: 2018-02-13

Review time: 4 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input 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 checked="" 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 checked="" 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

Shu-Rong Xiao et al. revealed antiviral effects of hepatitis B virus S gene-specific anti-gene locked nucleic acid in transgenic mice in this manuscript. English writing is well and this work is worth enough for possible publication in WJG if some comments



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listed below are properly responded. Major comments: 1. The legend of Table 1, 2 and Figure 2. ... transgenic mice (n=6, mean±SD) is ... transgenic mice (n=6, mean±SE) according to the description in Statistical analysis. 2. There are four control groups in this experiment. However, the definition of control groups is obscure. Anti-S-LNA group is a kind of positive control. The author should describe the definition of each group more precisely. 3. Immunohistochemistry shown in Figure 3 is not specific. It seems to be so hard or even impossible to quantify the positive signals corresponding to HBsAg in this picture. Please explain in details how the authors quantified the HBsAg-positive cells.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ [Y] No

BPG Search:

- ☐ The same title
- ☐ Duplicate publication
- ☐ Plagiarism
- ☐ [Y] No

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 38083

Title: Antiviral effects of hepatitis B virus S gene-specific anti-gene locked nucleic acid in transgenic mice

Reviewer's code: 00052926

Reviewer's country: Greece

Science editor: Xue-Jiao Wang

Date sent for review: 2018-02-02

Date reviewed: 2018-02-16

Review time: 14 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input 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

The manuscript by Shu-Rong X et al on locked nucleic acid technology for the treatment of chronic hepatitis B on experimental animals (transgenic mice) describes a very interesting and promising work. The researchers developed an anti-gene locked nucleic



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acid (LNA) targeting HBV S gene while being resistant to nuclease degradation. A high antiviral effect was achieved with reduction of HBsAg, HBV DNA levels in a time-dependent manner, a reduction of HBV S gene expression levels and HBsAg positive cells in the liver of sacrificed animals. The manuscript is original, well designed and well written. However, it would be useful for the authors to describe first the advantages of this novel approach versus the classical anti-sense oligonucleotide approach. Second the limitations of the study should be mentioned. Third it would be useful to consider the possible constraints in order to apply this method in humans.

INITIAL REVIEW OF THE MANUSCRIPT

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- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 38083

Title: Antiviral effects of hepatitis B virus S gene-specific anti-gene locked nucleic acid in transgenic mice

Reviewer's code: 00503536

Reviewer's country: Japan

Science editor: Xue-Jiao Wang

Date sent for review: 2018-02-19

Date reviewed: 2018-02-22

Review time: 2 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 checked="" 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

The manuscript written by Shu-Rong X et al. describe the antiviral effect of hepatitis B virus (HBV) S gene-specific anti-gene locked nucleic acid (LNA) in transgenic mice. LNA significantly suppressed HBV S gene expression, and decreased serum HBsAg and HBV

DNA. Although nucleotide analogs have been used as effective therapeutic agents for the control of HBV infection, this novel approach could provide another promising strategy for the control of HBV. However, there are some serious concerns that need to be addressed. Major points, 1. The characteristics of HBV transgenic mice, such as transgene and genetic background, are unclear. Moreover, histology of the liver show positive for cytoplasmic HBsAg in all hepatocytes, which is quite different from other HBV transgenic mice (Guidotti LG, Matzke B, Schaller H, Chisari FV. J Virol. 1995 Oct;69(10):6158-69). The authors should describe on those points. 2. Serum HBsAg and HBV DNA were assessed only 7 days after treatment, and it is unclear how long the inhibitory effect of LNA last. 3. The kinetics of HBV DNA in addition to that of HBsAg gene should be shown. Minor point 1. The effect of combination therapy with lamivudine and LNA would be interesting. 2. Immunohistochemical data on HBcAg in the nuclei of hepatocytes with each treatment would be interesting.

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