



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 38396

**Title:** Detection of hyper-conserved regions in hepatitis B virus X gene potentially useful for gene therapy

**Reviewer's code:** 02942902

**Reviewer's country:** Japan

**Science editor:** Xue-Jiao Wang

**Date sent for review:** 2018-02-17

**Date reviewed:** 2018-02-23

**Review time:** 6 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 polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The authors collected sera of HBV-infected patients with various clinical conditions and analyzed the DNA sequences of HBx region by means of the next generation sequencing (NGS) technique. They detected two nucleotide regions which were highly conserved



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regardless of the patients' clinical stage or HBV genotype. They concluded that these newly identified conserved regions could be potential targets for gene therapy. Overall, the manuscript is well-written and the results seem to be reasonable. I have some comments. 1) They identified two highly conserved regions. As they discussed, in vitro functional studies should be important to evaluate the potential usefulness of these domains as targets for siRNA-based antiviral gene therapy. However, the experimental study may be included in the next paper. I would like to know whether they consider "these two domains are equivalent" or "one of the domains can be more promising than the other one". 2) They used various/heterogeneous clinical samples and detected two conserved regions. However, HBx protein is suggested to relate to hepato-carcinogenesis. Did the NGS analysis provide any common variant among the patients who had hepatocellular carcinoma? (Did they find any mutation as a candidate for carcinogenesis-associated sequence in HBx region?)

#### **INITIAL REVIEW OF THE MANUSCRIPT**

##### ***Google Search:***

- The same title
- Duplicate publication
- Plagiarism
- No

##### ***BPG Search:***

- The same title
- Duplicate publication
- Plagiarism
- No