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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 28546

**Title:** The Development of Liver-targeted Hydrodynamic Gene Therapy: Mini-review

**Reviewer's code:** 00068723

**Reviewer's country:** Japan

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-07-06 17:46

**Date reviewed:** 2016-07-06 20:27

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

There are non-viral methods of gene delivery, such as sonoporation. This manuscript discussed hydrodynamic gene delivery. As compared with sonoporation, hydrodynamic gene delivery is relatively less-popular. This manuscript is informative and well-organized. System presented in Figure 2 is interesting. Is this computer-assisted injection system innovated by a company? Is this system commercially available? Or is this system build by the authors' institute? The authors proposed congenital disease as a potential clinical application. Do the authors think hydrodynamic gene delivery to hepatocellular carcinoma (HCC) as a potential target disease? If so, how do the authors restrict delivery of therapeutic genes to HCC?



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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 28546

**Title:** The Development of Liver-targeted Hydrodynamic Gene Therapy: Mini-review

**Reviewer's code:** 00504303

**Reviewer's country:** China

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-07-06 17:46

**Date reviewed:** 2016-07-18 16:10

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

This manuscript provides an extensive review on liver-targeted hydrodynamic gene delivery based gene therapy. Hydrodynamic delivery (HGD) is an efficient procedure to deliver numbers of nucleic acids to hepatic tissues. The successful application of hydrodynamic delivery is dependent on the rapid injection of a large volume containing nucleic acids into the liver. This review summarizes the HGD method principle, efficiency, safety, modification in large-animal models, and gene therapy in various diseases. The topic is of great interest to the field. The manuscript is very well written and easy to read. HGD method does have some effects on the immune system and activate certain immune response to some extent. The authors should address on that issue.



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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 28546

**Title:** The Development of Liver-targeted Hydrodynamic Gene Therapy: Mini-review

**Reviewer's code:** 00646260

**Reviewer's country:** Spain

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-07-06 17:46

**Date reviewed:** 2016-07-18 16:54

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

The manuscript is interesting and the authors are specialists in the topic. It is written correctly and we think it could be interesting for the readers of World Journal of Gastroenterology. However, some questions should be considered. Major question: authors did not fully focused the manuscript on describing the development of liver-targeted hydrodynamic gene therapy but payed more attention on their own system for controlled gene delivery, which is an interesting delivery system. Thus, title should be modified in order to adjust to the major content of manuscript. Minor question: the format of reference 27 is not correct, family name of authors is not complete



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## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 28546

**Title:** The Development of Liver-targeted Hydrodynamic Gene Therapy: Mini-review

**Reviewer's code:** 00069130

**Reviewer's country:** United States

**Science editor:** Ze-Mao Gong

**Date sent for review:** 2016-07-06 17:46

**Date reviewed:** 2016-07-21 16:53

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" 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"/> The same title	<input type="checkbox"/> High priority for publication
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

Good review-useful for scientists and clinicians who are interested in gene therapy. The authors may also include a section compiling the existing data on HGD, comparing the efficiency of different studies (in the literature on HGD). This may inturn be compared with the efficiency of various other gene delivery systems (lentivirus, retrovirus, AAV etc). A table would be useful.