

ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6556

Title: Gene therapy for preventing liver cirrhosis, where we are?

Reviewer code: 00001541

Science editor: Ya-Juan Ma

Date sent for review: 2013-10-24 22:53

Date reviewed: 2013-11-09 20:23

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"/> Existed	<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 checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The work by Kim and Park is a revision on Gene therapy for preventing liver cirrhosis of poor quality. The paper has an inappropriate title as it only considers treatment based on ODN, siRNA, miR and decoy ODN, but not other gene therapy approaches such as gene therapy vectors encoding hepatoprotective and antifibrogenic cytokines (such as IGF-I or HGF). Also the consideration that pure blockade of pro-fibrinogenic factors could improve the liver lesion is quite simplistic. In chronic liver damage not only matters the increased ECM but also the compromised hepatocellular function. Any effective therapy should correct both aspects. There are also a number of overstatements concerning the relevance of the ODN-based therapies and little critical consideration of the problems related to the use of this approach in the clinic. Some expressions are incorrect: miRNA are not a sort of natural ODN since RNA molecules are not oligodeoxynucleotides.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6556

Title: Gene therapy for preventing liver cirrhosis, where we are?

Reviewer code: 00071472

Science editor: Ya-Juan Ma

Date sent for review: 2013-10-24 22:53

Date reviewed: 2013-12-17 10:38

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"/> Existed	<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 checked="" type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The authors reviewed targeted strategies for the treatment of liver fibrosis, and particularly, targeted gene therapy using ODNs. 1. The paper is confusing because; The paper only covered oligonucleotide-based therapy, not other gene therapy, which is not consistent with the title The paper reviewed oligonucleotide-based therapy for liver cirrhosis, which means for curing liver cirrhosis, not preventing liver cirrhosis. If for preventing liver cirrhosis, it should be given before cirrhosis stage. the This is a good summary that can be useful for scientist and clinicians in the field. The manuscript is well organized and well written. However, the following minor changes has to be made; 2. I suggest the authors to provide summary of important findings or researches in Table for for each topic. 3. The authors should discuss about advantages and disadvantages of those gene therapies. 4. Please note that miRNA and siRNA are not ODN. The authors should be carefully use the term of "ODN".

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6556

Title: Gene therapy for preventing liver cirrhosis, where we are?

Reviewer code: 00159305

Science editor: Ya-Juan Ma

Date sent for review: 2013-10-24 22:53

Date reviewed: 2014-02-16 21:44

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 checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input checked="" 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)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

To the authors, Congratulations for this review. The manuscript is well written and has no major flaws. I have some (relatively minor) concerns, as listed below: 1. Abstract: a. no need to abbreviate oligodeoxynucleotides. b. Last phrase , (for the treatment of liver fibrosis) should be liver cirrhosis (see the title of the review). 2. Introduction: a. Page 4, second and third phrases : please, make them more clear b. Page 4 first paragraph, last word: fibrogenesis or fibrosis? 3. Gene therapy and all over the text: a. There are too many abbreviations which make difficult to keep readers attention (e.g. in one single page there are nearly 50 abbreviations!) b. Page 5, second paragraph, last phrase: "recently.....@ the article was published more than a decade ago!!! c. Tables 1 and 2 are not included in text!?? 4. Conclusion section: a. Is too long, please rewrite it. b. Please delete "table 2...", " for example" (twice on page 13) c. You repeat three times "small RNA - and DNA-based therapeutics" in two consecutive paragraphs (page 13 and 14) 5. References: please, refer to the authors' instructions (e.g. first author underlined) 6. Figure 1: is it original? If not, please cite the reference including permission for reproduction .

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6556

Title: Gene therapy for preventing liver cirrhosis, where we are?

Reviewer code: 00199518

Science editor: Ya-Juan Ma

Date sent for review: 2013-10-24 22:53

Date reviewed: 2014-02-17 01:40

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

A good review on future perspective in patients with liver cirrhosis. English language needs improvement.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6556

Title: Gene therapy for preventing liver cirrhosis, where we are?

Reviewer code: 02438768

Science editor: Ya-Juan Ma

Date sent for review: 2013-10-24 22:53

Date reviewed: 2014-02-17 19:12

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"/> Existed	<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)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Comments for ESPS Manuscript NO: 6556 1. General comments Liver fibrosis can be viewed as a disease in which multiple genes interact with environmental factors. Advances in understanding of the pathogenesis of liver fibrosis have identified several potential therapeutic approaches. Among them, gene therapy seems to be feasible in the treatment of liver fibrosis. In this manuscript, the authors focused on the experimental approaches of small RNA- and DNA-based gene therapy for liver cirrhosis. This manuscript is well-organized in structure and rich in content. I would like to recommend authors to respond to the following comments. 2. Specific comments a) Major comments: # Although gene therapy has a therapeutic effect in experimental animal models of liver fibrosis, it is more necessary to elucidate whether gene therapy is also effective for liver fibrosis in humans. In my opinion, the above topic should be addressed in the manuscript. # Gene therapy can simultaneously induce cytotoxic effects while treating liver fibrosis, which in turn affects the recovery of liver function. In addition, the potential long-term side effects of gene therapy remain to be elucidated. One major concern with gene therapy has been its propensity to cause cancer. For example, random integration of the therapeutic genes into the host genome could either activate nearby oncogenes or inactivate tumor suppressor genes, and therefore induce cells to malignant transformation. This may occur not only in experimental animal models, but also in humans. Has there been any research progress in overcoming these obstacles? In my opinion, these topics should also be explored in the manuscript. b) Minor comments: The minor comments are omitted.

ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6556

Title: Gene therapy for preventing liver cirrhosis, where we are?

Reviewer code: 00006992

Science editor: Ya-Juan Ma

Date sent for review: 2013-10-24 22:53

Date reviewed: 2014-02-17 22:59

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

During the review process the paper by Kim and Park has been improved impressively. Including of the two tables - Summary of studies using small RNA and DNA based therapies in liver cirrhosis - Advantages and disadvantages of small RNA- and DNA-based gene therapy Improved the review article considerably. Changing of title and eliminating lots of grammatical errors improved the revised version in addition. From my point of view the manuscript could be published now.

ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6556

Title: Gene therapy for preventing liver cirrhosis, where we are?

Reviewer code: 00503530

Science editor: Ya-Juan Ma

Date sent for review: 2013-10-24 22:53

Date reviewed: 2014-02-26 07:19

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"/> Existed	<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)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The author searches many documents and gathers it up carefully. I have a question to ask you. How about the start time of the treatment to hold liver fiberization in check by a gene therapy? If the sustained infection of the hepatitis virus is established, will you perform it? Or is it after a diagnosis of the chronic hepatitis? May the fiber ingredient be eliminated? Is the gene therapy that I limited to liver cancer considered?