Author's response to reviews

**Title:** Autoantibodies against Angiotensin II Type 1 Receptor-positive Patients with Heart Failure Have Better Clinical Efficacy to Perindopril Treatment

**Authors:**

- Qian Du (duqian1213@126.com)
- Xin Wang (wangxinpeking@126.com)
- Zhi yong Zhang (zhangzhiyongpeking@126.com)
- Lin Xu (xulinpeking@126.com)
- Juan Zhang (zhangjuanpeking@126.com)
- Hua Wang (wanghuapeking@126.com)
- Jin Chen (chenjinpeking@126.com)
- Hakon Hakonarson (HakonarsonHakon@126.com)
- Ai hua Hu (huaihuapeking@126.com)
- Lin Zhang (Linzhangpeking@126.com)

**Version:** 5  **Date:** 6 July 2013

**Author's response to reviews:** see over
Dear editor:

Firstly, we would like to express our sincere thanks to the reviewers for the constructive and positive comments. We have substantially revised our manuscript after reading the comments. We employed an English-language editor service to polish our word. We also expanded part of discuss, providing details in the current version, and the amendments are in the revised manuscript. Point by point response to the reviewers’ comments is listed below this letter.

This manuscript has been edited and proofread by Scientific Writing Solutions USA Limited.

We hope that the revised version of the manuscript is now acceptable for publication in your journal.

I look forward to hearing from you soon.

With best wishes,

Yours sincerely

Lin Zhang

Professor

Corresponding author
Answers to reviewers:

Reviewer #1

We thank the reviewer for these very useful comments. We have considerably revised the manuscript for clarified; I have made every effort to address the specific comments below.

**Q1. If I understand correctly this should be:** Perindopril treatment promote left ventricle remodeling in patients with heart failure screened positive for autoantibodies against angiotensin II type 1 receptor. Two duplicated sentences in methods (Anti-AT$_1$-AR determination).

**Answers:** We fully agree with the reviewer and apologize for these mistakes. We have deleted those duplicated sentences in the revised manuscript. (Page 7, line 107-121)

**Q2. Authors should clarify what is blank and what is negative control (sample OD - blank OD/negative control OD - blank OD) since this is an in-house EIA …**

**Answers:** We thank the reviewer for these very useful comments. We have included this information in the revised manuscript. (Page 7, line 136, Page 9, line 180)

**Q3. Positive sera for AT1 receptor in CHF was 56.41 % (88/156), significantly**
higher than that in the control group. Authors should describe the aforementioned control group. I cannot see any data on this group in patients section or in table 1.

**Answers:** Our series of studies showed that in the normal population AT1 autoantibodies titers was about 11.9%, the reference of this report is attached in the attachment, and the article is in Chinese. Normal population was the control group.

**Q4** Authors should discuss more on the potential pathogenic/beneficial role of anti-angiotensin II type 1 receptor autoantibodies. What happens in the group of patients with autoantibodies disappearance or significant titer reduction (>4 fold) regarding primary outcome and LV remodeling? Also, some more discussion on the mechanisms of titer reduction or disappearance upon perindopril treatment would be appreciated. English must be improved throughout the manuscript.

**Answers:** We thank the reviewer for these very useful comments. We read the literature and have modified the text based on your comments in the manuscript accordingly. (Page 11-15, line 236-334)

**Minor revisions:**

Many typing and formatting errors throughout the manuscript. References should be uniform in terms of formatting (Journal abbreviations). Level of interest: An article of importance in its field.
Answers: We apologize for the errors. We have modified the text and uniform the references in terms of formatting.

Reviewer #2:

Reviewer's report

Title: Autoantibodies against angiotensin II type 1 receptor-positive patients with heart failure have better clinical efficacy of perindopril treatment

Version: 4 Date: 19 April 2013

Reviewer: jianming Zhi

Reviewer's report:

good

Level of interest: An exceptional article

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

No

Answers: Our study had some limitation and shortages, thank the reviewer for the positive assessment of the manuscript. We have substantially revised our manuscript after reading the literature and comments, polish our word by English-language editor. We also expanded part of discuss, providing details in the current version, and the
amendments are in the revised manuscript. Please don't hesitate to contact us if you have questions or suggestion regarding my manuscript.

functional changes in the primary heart disease. Each autonounboby, which consists the above three receptors, may play an important role in the pathogenesis and myocardial remodeling of heart failure with different heart diseases.

【Key words】Heart failure; congestive; Receptors adenomergic; beta-2; Receptors adenomergic; alpha-1; Receptors angiotensin; Autonounboby

Recently, many scientific investigators in the expansion pattern heart muscle heart force衰竭(心衰) patients have observed the existence of a protein complex in the plasma, consisting of M,-adenomergic receptors and adenominergic receptors. This complex is thought to play a major role in the pathogenesis and remodelling of heart failure with different heart diseases.

Aim: To investigate the role of these receptors in the expansion pattern heart muscle heart force衰竭(心衰) patients.

Methods: Thirty expansion pattern heart muscle heart force衰竭(心衰) patients were included in the study. The study was conducted at the Heart Failure Clinic, University Hospital, and the results were compared with a control group of 30 normal subjects.

Results: The expansion pattern heart muscle heart force衰竭(心衰) patients had significantly higher levels of M,-adenomergic and adenominergic receptors compared to the control group. The results also showed a significant correlation between the levels of these receptors and the severity of heart failure.

Conclusion: The results of this study suggest that the M,-adenomergic and adenominergic receptors play a significant role in the pathogenesis and remodelling of heart failure with different heart diseases.

Table 1: 2006 Overview of Heart Failure Patients in the Clinic (N=30)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD</td>
<td>40</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>DCM</td>
<td>45</td>
<td>20</td>
<td>25</td>
</tr>
<tr>
<td>HBF</td>
<td>38</td>
<td>18</td>
<td>20</td>
</tr>
</tbody>
</table>

Notes: N=30; SD=0.1