Authors' Response to Reviewers' questions/suggestions related to *39573-Manuscript*

Dear Editor,

Thank you very much for this opportunity to revise and improve our manuscript. The revised manuscript is now amended accordingly. We addressed all your questions indicated in the 39573-edited file and all questions suggested by three reviewers. All three figures were graphically improved in the revised version of the manuscript.

Reviewer 1

"... It seems like figure 1 describing about the S1P2 receptor signaling mediated by Gi protein in page 10 and Figure 1 describing about SphK/S1P signaling leading to several different cell singling are different. Please re-check them carefully"

The Author's response to Reviewer 1;

Thank you very much for your review and kind comments. The mistake is now corrected in the revised version of the manuscript. The correct figure 1 is now included.

Reviewer 2

"... Some typographic errors: hall mark.....hallmark (page 1) TGFb..... TGFbeta (greek) , TNFa...alpha(greek) (page 2) hemopoietic.....hematopoietic (page 3, 4) Stat is not " Activator of Transcription". Stat is a "Signal Transducer and Activator of Transcription" (page 8 and 10) key stone.....keystone (page 9)"

The Author's response to Reviewer 2;

Thank you very much for your review and high evaluation of our work. All detected mistakes were corrected in the revised version of the manuscript.

Page 1: "hall mark" was replaced with "hallmark"

Page 2: in TGFb amd TNFa - alpha and beta were replaced with the Greek letters

Pages 3 and 4: "hemopoietic" was replaced with "hematopoietic"

Pages 8 and 9: " Activator of Transcription" is now extended to "Signal Transducer and Activator of Transcription"

Page 9: "key stone" is replaced with "keystone"

Reviewer 3

"*… Points to be corrected:*

1) In line 2 in page 15, "Figure 1" should be corrected as "Figure 3". Also, the title of this Figure should be corrected. 2) The Figure 2 in page 15 should be deleted since it is a

duplication of Figure 2 in page 13. 3) There is no sentence that refers Figure 2. Please add some descriptions. An example is shown in page 12 in "modified 39573-Manuscript File". 4) The format of Figure 1 is distinct from that of Figure 2. It is desirable for authors to revise the Figure 1 according to the format of Figure 2. An example is attached to page 10 in "modified 39573-Manuscript File". 5) Additional points that need modification are shown in "modified 39573-Manuscript File

The Author's response to Reviewer 3;

Thank you very much for your review and high evaluation of our work. We highly appreciate your impact and detailed corrections of our manuscript. All detected mistakes were corrected in the revised version of the manuscript as following;

1) page 15 (line 2), "Figure 1" is now cited as "Figure 3"; the figure title is now corrected;

2) The Figure 2 in page 15 was deleted;

3) Figure 2 is now cited on page 12 (as you recommended), and on page 11 and 15 (where it is considered as appropriate).

4) The format of Figure 1 is now adjusted according to your suggestion. We are very thankful for your kind effort to improve our work!

5) All additional points were addressed according to your editing.

Kind regards,

Mei Li Ng, PhD

Mario Menschikowski, PhD

Nagendra S. Yarla, PhD

Olga A. Sukocheva, PhD