Author’s response to reviews

Title: Effects of resveratrol on Th17 cell-related immune responses under tacrolimus-based immunosuppression

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Author’s response to reviews:

Dear Prof. Hokeun Kwon

Editor-in-Chief, BMC Complementary and Alternative Medicine

Thank you very much for the evaluation of our manuscript. We are returning a revised manuscript which incorporates many of the suggestions made by reviewers. A response to the referees’ suggestions has been listed one by one, and an index of change has been included. We hope that the comments of the referees are adequately addressed in the revised manuscript.
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Index of changes

Major changes:

1. Addition of the sources, tradename, company, city and country of the reagents in Methods.
2. Clarification of the Th17 polarization condition
3. Addition of important reference and also discussion about it

Minor changes

1. Correction of reference format

Sincerely yours,

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Response to Editor's Comments to Author:
<Reviewer 1>

The effects of Resv under Tac-treatment conditions, on CD4+ T cell differentiation to Th17 cells in PBMC, and proliferation of CD4+ T cells cocultured with human renal proximal tubular epithelial cells (HRPTEpiCs). Resv provides additional immunosuppressive effects to Tac by suppressing effector CD4+ T cells, especially Th17 cells, in the transplantation setting. This job suggests that Resv can be used as a therapeutic agent to complement the effects of Tac-based immunosuppression in organ transplantation, it is very meaningful.

→ Thank you for your comments.

<Reviewer 2>

It is an intriguing study of the resveratrol effect on Th17 cell-related immune responses in the presence of tacrolimus (an immunosuppressive drug), in the mimic transplantation status using PBMCs, HRPTEpiCs (human renal proximal tubular epithelial cells lines), Jurkat cells in vitro, whether in vivo and ex vivo model (xenograft using allograft in mice). It is a novel finding of explanation of the mechanism of resveratrol on enhanced immune suppression together with tacrolimus. The signaling pathways were also clarified to be via AMPK and mTOR phosphorylation pathway.

However, the report should include of the sources, tradename, company, city and country of the reagents in Methods.

→ Thank you for your comments. We added the sources, tradename, company, city and country of the reagents in Methods. (Methods section page 4 ~ 11)

The authors used the Real-time RT-PCR, it did not need to add Real-time PCR again in the following sub-topic.
Thank you for your comments. We omitted the duplicated "real-time PCR".

(Methods section, line 15, page 8)

The polarization should be more clarified and described. The conditions or species or sources of each cell should be emphasized, which mimic transplantation in human-beings or mammals, in vitro, in vivo and ex vivo.

Thank you for your comments. In an in vitro study, we used well established Th0 or Th17 polarization condition which has been used in previous studies including our own. (Ref [11], [12], [21])

The cells used in the in vitro study were isolated from healthy volunteers. In the western blotting to investigate the pathway involved in the suppressive effect of Resv, we used Jurkat cell line. (ATCC, Manassas, VA, USA)

We added above information in the revised manuscript.

(Methods section, line 17, page 5), (Methods section, line 6, page 6)

Discussion part should be added with the research works of Jang GR & Harris RZ, 2007: Drug interactions involving ethanol and alcoholic beverages, about the polyphenols in alcohol interaction resulting in hepatotoxicity.

Thank you for your comments. We added above article as reference, and also discussed the content in the discussion.

(Discussion section, line 17, page 19)
Minor points:

Every full name should be mentioned first and abbreviated form in the brackets. Reference format: especially the journal name: some are in full and some are abbreviated. It should be strictly according to that of the journal's form.

→ Thank you for your comments. We corrected the abbreviated form (Abstract section, line 13, page 2) and we also corrected reference format.