

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2429-review.doc).

Title: Epigallocatechin-3-gallate suppresses transforming growth factor- β signaling by interacting with the transforming growth factor- β type II receptor

Authors: Masaki Tabuchi, Sumio Hayakawa, Eiko Honda, Kana Ooshima, Tatsuki Itoh, Koji Yoshida, Ah-Mee Park, Hideaki Higashino, Mamoru Isemura, Hiroshi Munakata

Name of Journal: World Journal of Experimental Medicine

ESPS Manuscript NO: 3683

1. Running title has been added.
2. Author contributions have been added.
3. One author has been added.

The manuscript has been improved according to the suggestions of reviewers:

1. The format has been updated.
2. The following revisions have been made in accordance with the suggestions of the reviewers.
3. The altered parts of the manuscript have been indicated in red font wherever possible.

Reviewer 00036517

- (1) We added a description of the MRC-5 cell line (page 5, line 30).
 - (2) We added sentences explaining the reason for the plasmid construction study (page 6, line 26). Some parts of methods section were also rewritten (page 3, line 17; page 5, line 19).
 - (3) The relevant part of the discussion was rewritten in more detail.
- Minor points; we included abbreviations after the name of the antibody.

Reviewer 00051227

- (1) We added a sentence to address the referee's comment (page 6, line 10). Figure 1 was also changed.
- (2) Some parts of the methods section were rewritten (page 3, line 17; page 5, line 19). We also described the solvent in which EGCG was dissolved (page 3, line 19).
- (3) We added a description of the MRC-5 cell line (page 5, line 30).
- (4) Abbreviations were not used in the title of the revised manuscript.

Reviewer 00503623

- (1) We have carried out an additional experiment and included new data indicating direct binding between EGCG and TGFRII (Abstract, page 2, line 14; Methods, page 5, line 19; Results page 7, line 1). We polished the 2nd and 3rd sentences in the abstract (page 2, line 6).

Reviewer 00742223

- (1) We usually add 1-2 ng/ml TGF- β to the culture medium on the basis of other studies; we have now cited relevant papers (page 6, line 2). We also did a dose-response

study with different concentrations of EGCG (Fig. 1B) and used the optimum concentration in subsequent studies. In addition, we have cited a paper describing the EGCG concentration used in a cell culture study. (page 6, line 9).

(2) We have now described the MRC-5 cell line (page 5, line 30).

(3) As described in the text (page 5), we carried out a binding experiment with positive data; thus, we think that an experiment using whole cells is not necessary.

(4) α -SMA is a reasonable and often used marker of myofibroblast activation.

We have clarified this point in the text, citing relevant references (page 6, line 3; page 7, line 23).

(5) We have now cited relevant papers examining myofibroblast activation of other fibroblastic cell lines (page 7, line 28).

Reviewer 02440441

We have carried out an additional experiment and included new data indicating direct binding between EGCG and TGFRII (Abstract, page 2, line 14; Methods, page 5, line 19; Results page 7, line 1).

References and typesetting were corrected

Sincerely yours,

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P.S.

Please find an attached certification.

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To whom it may concern:

An experienced medical editor whose first language is English has carefully reviewed this paper titled:

**Epigallocatechin-3-gallate suppresses transforming growth factor- β
signaling by interacting with the transforming growth factor- β
type II receptor**

Our company specializes in the editing of papers written by physicians and scientists whose native language is not English.



Shuji Ito

President NAI, Inc.