Author's response to reviews

Title: Genistein inhibits tumor invasion by suppressing multiple signal transduction pathways in human hepatocellular carcinoma cells

Authors:

Shulhn-Der Wang (wsd917@ms42.hinet.net)
Bor-Chyuan Chen (cbclez@gmail.com)
Shung-Te Kao (stkao@mail.cmu.edu.tw)
Ching-Ju Liu (chingju2006@gmail.com)
Chia-Chou Yeh (yehcc0530@gmail.com)

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Author's response to reviews: see over
Reviewers' comments:

Reviewer #1: Most of the revisions are adequate, however, the following additional corrections are required.

(1) In Abstract, the authors should mention the results of the two other hepatoma cell lines (Huh-7, HA22T) and murine embryonic liver cells (BNL CL2).
ANS: We add those results in the abstract.

(2) P5, L5: Reference citation should be identified by number.
ANS: We had corrected the error.

(3) P7, L1: The sentence "Cells were----24h." should be deleted.
ANS: we had deleted the sentence.

(4) P7, L5: What is complete media?
ANS: complete media is containing culture medium and drug. The sentence is redundant. The sentence was rewritten.
“HepG2 cells were resuspended with 100 µL in 96-well plates and cultured with or without 80 µM TPA and Gen, incubated for 24 h, then 20 µL MTT was added to each well and incubated at 37°C for 4 h.”

(5) P8, L10-11: What is NE?
ANS: Sorry! It is typing errors. The sentence was rewritten.
“Gelatin zymography was used for determination of expression and activities of MMP-9 in TPA-treated with or without Gen in human HepG2 cells. HepG2 cells were seeded in 100 mm plates using serum-free medium and pretreated TPA with different concentrations of Gen.”

(6) P9, L11: The author must use MMP-9-Luc plasmid-transfected cells as well as NF-κB-Luc and AP-1-Luc plasmid-transfected cells.
ANS: We add the part of MMP-9 in the sentence.

(7) P12, L3: Fig. 2A should be corrected to Fig. 2C.
ANS: We corrected the error.

(8) P12, L15-17: The authors should mention the results of BNL CL2.
ANS: We add the sentence to mention the results of BNL CL2.
(9) P13, L10: Why did the authors use the AP-1-transfected cells as control for the MMP-9 promoter assay?
ANS: Sorry! That was typing error. We had revised it.

(10) P14, L5, L8: Figure numbers are incorrect.
ANS: We had revised it. thanks.

(11) P22, L1-4: Figure parts, such as (A) and (B), should be explained.
ANS: we had add the explain in the legend.

(12) P23, L2-3: Did you incubate the MMP-9 purified from conditioned medium with Gen? If not, please correct the sentence.
ANS: The sentence was corrected. Thank your remind.

(13) P23, L9-10: Did you treat cells with Gen and then transiently transfected with plasmid? If not, please correct the sentence.
ANS: This is a typing error and the sentence was corrected. Thank your remind.

(14) Legend of Fig. 5: Figure parts, (A) - (E), should correctly be indicated. The procedure for determining translocation of NF-κB should be described in Materials and Methods.
ANS: We revised the Legend of Fig. 5 and 6, and then added the description in Materials and Methods.

(15) There are several grammatical errors, and thus I would prefer the authors to be assisted with language services.
ANS: A medical editor who is a native English speaker associated with MedCom Asia, Inc., has edited the manuscript.

Reviewer #2: 1.Although the authors added other 2 cell lines in the manuscript, there is still only one cell line(HepG2) used in this study to test the signaling pathways. It makes the conclusion seems still not reliable.
ANS: We added data of other 2 cell lines in the signaling pathways by EMSA and western blot. We expect to increase the credibility of the information.
2. AKT inhibitor (PTEN) (Sigma-Aldrich)? Do the author really know about the inhibitors or just “think out”? It's really a terrible false!

ANS: We are sorry about it. This is mislabeled of antibody. We re-order the antibody A6730 Akt1/2 kinase inhibitor from Sigma. We re-collected results containing with inhibitors.