Author's response to reviews

Title: Inhibitory effect of ginsenoside Rg3 combined with gemcitabine on angiogenesis and growth of lung cancer in mice

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Version: 4 Date: 1 July 2009

Author's response to reviews: see over
01–July–2009

Dear Editor,

In the revised manuscript, we asked a friend majoring in English to improve the language again (all modifications made are highlighted in orange). In addition, we replied to the questions of the referees. As to some suggestions such as incorporate the additional immunohistochemical data requested by Reviewer 1, we think that it’s true that these suggestions such as the apoptosis and KI-67 or proliferating cell nuclear antigen (PCNA) for IHC, etc would shed light on possible mechanisms behind Rg3. Unfortunately, in the revised manuscript, we did not add new data. China Wenchuan Earthquake (8.0 Richter Scale, 2008) in Sichuan province damaged our laboratory and our tissue specimen. Now, our laboratory is being repaired and decorated, and it will last at least two month. If we add some new data, we will prepare animal models again, and it will be a timely work. So, we feel sorry that we could not add some new data.

Sincerely yours,
Cheng Yi

Replies to Reviewer 3 (Cheryl Baker)

Title: Inhibitory effect of ginsenoside Rg3 combined with gemcitabine on angiogenesis and growth of lung cancer in mice

Version: 3 Date: 12 May 2009

Reviewer:

Reviewer's report:
Discretionary Revisions - the authors have addressed the reviewer's comments and must now make sure that the English is correct.

Level of interest: An article whose findings are important to those with closely
related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests

We asked a friend majoring in English to improve the language again.

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**Replies to Referee 1**

I previously recommended additional IHC. This is not an expensive or timely assay since they have the tissues to stain. Stain as suggested and resubmit. The additional IHC will shed light on possible mechanisms.

It's true that the apoptosis and KI-67 or proliferating cell nuclear antigen (PCNA) for IHC would shed light on possible mechanisms behind Rg3. China Wenchuan Earthquake (8.0 Richter Scale, 2008) in Sichuan province damaged our laboratory and our tissue specimen. Now, our laboratory is being repaired and decorated, and it will last at least two month. If we do apoptosis and KI-67 or PCNA for IHC, we will prepare animal models again, and it will be a timely work. In addition, the revised manuscript should be resubmitted by 6 July 2009. In one month, it is impossible to do apoptosis and KI-67 or PCNA for IHC. Thanks for your recommendation again. In our further study, we will consider your suggestions.

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**Replies to Referee 2 (Wanju Kim)**

**Reviewer's report:**

This paper has shown that synergic inhibitory effect of ginsenoside Rg3 and gemcitabine in vivo on the mouse.

Authors used such as color Doppler, measurement of tumor size, rate of necrosis tumor, immunohistochemistry with CD31 and VEGF and microvessel density.
Overall

3. Are the data sound?

Review opinion -- The authors must shown stronger evidence about inhibitory effect of angiogenesis and growth. Previous I gave some minor problems but authors never add new data for support their idea.

The purpose of our study is to evaluate the efficacy of low-dose gemcitabine combined with ginsenoside Rg3 on angiogenesis and growth of mice Lewis lung carcinoma. So, in this study, we observed tumor volume, inhibitive rate, necrosis rate, signals of blood flow and dynamic parameters of arterial blood flow in tumors as well as VEGF expression and MVD, etc. As to your suggestions such as immunoblot about cell cycle, apoptosis, necrosis, angiogenesis and signaling, immunoassaying with TUNEL assay in tumor tissues and caspase assay data, in vivo data such as invasion assay and MTT assay, etc., we think these experiments would be better to elucidate the mechanism behind low-dose gemcitabine combined with ginsenoside Rg3.

China Wenchuan Earthquake (8.0 Richter Scale, 2008) in Sichuan province damaged our laboratory and our tissue specimen. Now, our laboratory is being repaired and decorated, and it will last at least two month. If we add some new data, we will prepare animal models again, and it will be a timely work. In addition, the revised manuscript should be resubmitted by 6 July 2009. In one month, it is impossible to add new data. In our further study, your suggestions will be taken into our consideration. Thanks for your advice again.