Reviewer's report

Title: Therapeutic effect of the fruit hull of Gleditsia sinensis on lung inflammation in an LPS-induced acute lung injury model is associated with Nrf2

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Reviewer: Hye-Youn Cho

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Major Comments

1. The current manuscript addresses mainly the effect of an herbal medicine bearing anti-inflammatory effects. Authors corrected the title. However, 'therapeutic' and 'association with Nrf2' in the new title are not proper to be used based on the current observations. If they intended to exam the association of Nrf2 in the current setting, authors must apply Nrf2 KO mice for all the measurement including Figure 1. Differences from histology and bronchoalveolar lavage cannot support the association of FGS effect and Nrf2 pathway. Added data of Figure 4, Nrf2 and downstream gene expression, are detected not in the lung of their ALI model, but in a lung cell line, which also does not convince their conclusions. 'Therapeutic effect' needs to be replaced with 'Protective' or similar. Conclusion section needs to be modified accordingly.

2. At the end of the Introduction, authors wrote that ‘…per the experimental evidence, we propose that FGS can be developed as a therapeutic option for ALI.’ As pointed in the comment#1 above, authors’ results could suggest potential therapeutic effect of FGS in ALI but it is not enough to be proposed to be developed as a therapy. Please fix the sentence.

3. Animals used need to be better clarified in the Methods in terms of proper genetic nomenclature, gender, and genetic background while they cited a reference. Through this, authors do not need to describe their background in the text.

4. During the first round of the review, it was suggested to combine Figures 2B and 5B (lung inflammatory cells) and Figures 2A and 5A (lung histopathology) should be combined to compare phenotypes side-by-side between wild type and Nrf2 gene knockout mice while authors insist to leave them as is. The problem is that wild type mouse data used in Figures 5A are the same as those presented in Figures 2, and the histopathology of Figure 5B might be from the same animals or the same study used for Figure 2B. It is still uncooperative was of data presentation and I am not sure if data redundancy is allowed. I will leave this issue to Editors for decision.

Minor Comments

1. In Method of Abstract, ‘….and histologic and semi-quantitative RT-PCR
analyses of lung sections of NF-κB reporter or C57BL/6 mice that received an intra-peritoneal (i.p.).', does NF-kB reporter indicate NF-kB transgenic mice?. Please find the best description of these mice and rephrase it.

2. Abstract Results: …FGS post-treatment improved histologic changes…’. Clarify what histologic changes. Also describe ‘…to do so in Nrf2-KO mice’. As the resolution of the lung sections in Figure 5A is not high enough to discuss many changes (just by viewing alveoli sections), authors should focus simply on cellularity. Also in Figure 2B, edema is evident in b but not much in d: I am not sure if protein level does not differ between LPS and LPS+FGS.

3. Please delete scale bar from Figures 2A and 5A and p value from Figure 3. They should appear in the Figure legend.

**Level of interest**: An article of limited interest

**Quality of written English**: Needs some language corrections before being published

**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.