Dear Professor Luo

Your letter of 14th of Aug 2019, together with the comments of reviewers to our manuscript (Manuscript ID: molecules-574039) entitled “Unraveling The Molecular Mechanism of Traditional Chinese Medicine Against Acute Viral Infections of Airway”, was received. Thank you very much. We are very grateful and thank reviewers for these kind corrections and suggestions. We have revised our manuscript according to these comments point by point. We have also asked a native English speaker to check the grammar and font of text thoroughly. Now, we are glad to send the revision of our manuscript to you.

*Molecules* is the leading international peer-reviewed open access journal of chemistry. We supposed that our work could improve the understanding of the mechanisms of herbal medicine and TCM. We hope that our answers are satisfactory. We would be most grateful if our manuscript could be considered for publication in the *Molecules*. Thank you very much.

Sincerely Yours,

Jung San Chang

Aug 26th, 2019
Response to the reviewer 2:

1. Generally speaking, this is an interesting and potentially valuable paper, especially if observed from the aspects of integrative medicine. However, to fulfill such expectations two chapters should be added: positioning TCM within modern concepts of integrative medicine, preferably addressing pathophysiology of oxidative stress describing relationships between herbal and non-herbal TCM treatments such as acupuncture.

Ans: We would like to thank reviewer for this valuable suggestion. We completely agree that positioning TCM within modern concepts of integrative medicine need to address oxidative stress in relation to herbal and non-herbal TCM treatments such as acupuncture. We have stated in section 2 “TCM includes herbal therapy, acupuncture, massage, and dietary therapy. In the current work, TCM will be simply defined as the herbal and dietary therapies”. Acupuncture is an important part of TCM. Its effect involves anti-oxidation pathway, neuroprotective, and anti-inflammatory processes [1]. Acupuncture has been proven to decrease inflammatory factors, such as TNF-α, IL-1β, IL-6, COX-1, COX-2 and PGE2 expression [2-4]. However, the current work focuses on the herbal and dietary therapies. Therefore, we did not include acupuncture. As for oxidative stress, it is quite important to clarify herbal treatment in relation to oxidative stress. Therefore, we have supplemented a section 5.6 Pitfall of interpretation of benefits, as follows:

Several health benefits of herbal medicine and TCM are claimed; for example, herbs and TCM formulas, including those discussed above, are believed to have anti-oxidative activities helpful against several diseases. This idea is based on reactive oxygen and nitrosative species (ROS/RNS) as metabolic byproducts that can cause damage to cellular macromolecules; thus, many diseases can be triggered by oxidative stress under high levels of ROS/RNS. These diseases include cancer, inflammation, and degenerative diseases. Oxidative stress causes damage either with an overwhelming production of ROS/RNS or under insufficient levels of antioxidants or repair mechanisms, so blocking the generation of ROS/RNS might prevent and/or manage these diseases [143]. However, ROS/RNS are also signaling molecules for several physiological functions, including regulation of vascular tone, control of ventilation and erythropoietin production, etc. Actually, ROS-mediated responses may protect against oxidative stress [144]. Besides, ROS/RNS may play a dual role in different diseases, i.e. ROS/RNS might contribute to or counteract the disease progression. It remains unclear that more dosage of antioxidants is not better and may even worsen a medical condition [143]. There
are insufficient data to establish the ability of TCM to decrease ROS/RNS levels and establish its effects on the disease, and this affects the interpretation of any claims of benefit. To validate such claims of the benefits of herbal medicine and TCM, much work remains to be done.

We would like to thank reviewer gratefully for the kind reminding and suggestions. We hope that our answers are satisfactory. Thank you very much.

References
144. Dröge W. Free radicals in the physiological control of cell function. Physiol Rev. 2002 Jan;82(1):47-95