Reviewer’s report

Title: Cold exposure induced oxidative stress and apoptosis in the myocardium by inhibiting the Nrf2-Keap1 signaling pathway

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Reviewer: Benzhi Cai

Reviewer’s report:

Dear authors,

The manuscript entitled: "Cold exposure induced oxidative stress and apoptosis in the myocardium by inhibiting the Nrf2-Keap1 signaling pathway" focused on whether exposure to cold weather was associated with infaust cardiovascular responses and its underlying mechanism. This manuscript was written logically, and the background and significance were well discussed. It was an interesting manuscript. However, there were still a couple of concerns that need to be addressed.

1. First of all, line 20-21, page 3, Mice and cold exposure model, Methods. "Thirty 8-10 w old Kunming mice were were obtained from Liaoning Provincial Laboratory Animal Public Service Center (China, Benxi city)."

There were double "were" in this sentence, and an extra "RETURN KEY" after "Liaoning". The authors should correct these mistakes.

2. Second, line 26-29, page 4, Real-time quantitative PCR analysis. "Bad 5′-CAGGCCTCCTGTGGGAC-3′ (forward), 5′-GGTAGGAGCTGTGGCGACT-3′(reverse); Nrf2 5′-GCCTGAGAGCTGTAGGCCC-3′ (forward), 5′-GGAATGGAAAATAGCTCCTGCC-3′ (reverse); Keap1 5′-AAGGAACATGATATGCCCTGACA-3′ (forward), 5′-ACACAGGCCCGCTCCAT-3′ (reverse)".

The authors should carefully recheck the sequences of these above primers. As when we checked the primer sequences of Bad, Nrf2 and Keap1 on the website of Primer-BLAST (NCBI), we found that the sequences could not match these genes, so the authors had better confirm these primer sequences once again.

3. Third, line 55-56, page 5, Cold exposure increased apoptosis in the myocardium. Since apoptosis can be triggered as a result of oxidation, the authors had better detect the expressions of both pro-apoptotic proteins and anti-apoptotic proteins in myocardium under cold exposure. Therefore, it is better to detect and analysed the pro-apoptotic proteins Bax and anti-apoptotic protein, for example Bcl-2.
4. Fourth, it is better to cite some new literatures. For example, Cui G, Luk SC, Li RA et al., J Cardiovasc Pharmacol 2015;65(1):39-46. Yin K, Zhao L, Feng D et al., Cell Physiol Biochem 2015;35(6):2451-62. It would seem discussing the current data as they related to the findings of these reports may be of value.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

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