Author's response to reviews

Title: Differential apoptosis gene expression of rhabdomyosarcoma cells in response to enterovirus 71 infection

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Author's response to reviews:

Dear editor:

We really appreciate you and reviewers for carefully reviewing our manuscript entitled “Differential apoptosis gene expression of rhabdomyosarcoma cells in response to enterovirus 71 infection” (MS: 9814499007542029) and giving us highly positive evaluation, helpful comments and constructive suggestions. Based on the reviewers’ helpful comments and constructive suggestions, we have revised the manuscript according to the reviewers’ suggestions. The point-to-point responses for reviewers’ concerns were also enclosed in this letter. We believe that the quality of the revised manuscript was greatly improved under the help of the reviewers. Meanwhile, we hope that the revised manuscript will be satisfactory and acceptable for the publication in BMC Infectious Diseases.

Sincerely yours

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Response to Referee 1: Prof. Minetaro Arita

Comment 1: Unfortunately, no experimental data was provided in this study to support the hypothesis or suggestions of the importance of the expression profile given in Discussion.

Response: Thanks the reviewer for this comment. We have added some experimental data with the expression detection of FasL, caspase-10, - 8, -7, -3, AKT2, JNK1/2, c-Jun and NF-κB by western blotting. We found that TNF superfamily proteins such as FasL, CD40L and TNF-κ were significantly up-regulated and the apoptosis-related cysteine proteinases including caspase-10, -8, -7 and -3 were activated at 20 h postinfection. Furthermore, EV71 infection also induced the phosphorylation of AKT2, JNK1/2, c-Jun and NF-κB at 20h postinfection.

Major compulsory revisions:

Comment 1: Many of the references are wrongly cited in this manuscript. The authors should check the reference again, and cite the original references.

Response: We have carefully checked the manuscript again and modified the reference citation in the revised manuscript.

Comment 2: Discussion is too lengthy and not summarized. A model that explains the observed expression profile in these apoptotic genes should be given in a new Figure to help the readers.

Response: Thank the reviewer for this comment. We have modified the discussion section with the deletion of some unnecessary parts. According to PCR array and western blotting, we have deduced the pathways and added a new Figure 8 for the better understanding of readers.

Response to referee 2: Prof. Angel Galabov

Comment: In the chapter ?Background? the position of EV71 in the human enterovirus A species has to be indicated. Some additional references could be included underlying the pathogenic role of EV71 as a causative agent several epidemic outbreaks (vs. page 1, line 6).

Response: Thank the reviewer for this constructive comment. We have modified the paragraph as “ EV71 is a member of Picornaviridae family composed of a large number of small non-enveloped, positive strand RNA viruses with a genome size of approximately 7.4 kb. Both EV71 and coxsackievirus A16 (CVA16) belong to the human enterovirus A species, which are major causative agents causing hand, foot, and mouth disease (HFMD) in children. However, patients infected with EV71 are liable to cause aseptic meningitis, encephalomyelitis, pulmonary edema and death. EV71 was first identified in
1969 in California when it was isolated from the feces of an infant suffering from encephalitis. Subsequently, EV71 infection is widely popular in many countries and regions, such as Taiwan, Singapore, Malaysia, and Hongkong, as well as Mainland in China. Up to now, the molecular pathogenesis of EV71 infection is still elusive.” Additionally, we have added some references underlying the pathogenic role of EV71 as a causative agent several epidemic outbreaks in Background.