Author's response to reviews

Title: The expression of p-ATF2 involved in the chondeocytes apoptosis of an endemic osteoarthritis, Kashin-Beck disease

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Author's response to reviews: see over
Dear editor,

Thank you for your letter. I greatly appreciate both your help and that of the referees concerning improvements to this paper. I hope that the revised manuscript is now suitable for publication. The revised parts of the paper are indicated in the manuscript in blue. Here, we are mainly writing our answer for the reviewers’ comments.

Reviewer: Francisco J Blanco:

1. A graphic showing the effect of different concentrations of T2 toxin in cell apoptosis must be included, as well as the effect of different concentrations of the p38 and ATF2 inhibitors.

Response: Thank you again for your suggestions to improve this paper. Actually, we used p38 and JNK inhibitors, and the results of the effect of different concentrations of the p38 and JNK inhibitors were provided. Moreover, the T-2 toxin as an environmental factor and the influence of an original nano-selenium (reference 38) on the T-2 toxin induced chondrocytes apoptosis will be investigated in our further studies.

2. Figure 2 B is not necessary, authors must to show morphologic changes characteristic of apoptosis. Then DAPI stain or Electronic Microscopy can show the apoptotic nuclear and cytoplasmic changes.

Response: Thank you for your advices and we omitted Figure 2B. For the long-term research on the pathology of KBD, we had published papers about the apoptotic phenomena of KBD chondrocytes.

![Identification and verification of differentially expressed proteins and the function study in Kashin-Beck disease cartilage. A dissertation submitted to Xi'an Jiaotong University for the degree of Doctor of Medicine by Weijuan Ma. Fig 2.2 Electronic microscopy of normal chondrocytes (C) and KBD chondrocytes (D)(×6000).](image-url)

Fig. 4. Apoptotic morphological changes in the nuclear chromatin of cells were detected by Hoechst 33258 staining. Normal chondrocytes (A ×200 and C ×400) showed the majority of cells had uniformly stained nuclei, KBD chondrocytes (B ×200 and D ×400) showed the morphological changes typical of apoptosis (i.e., smaller and brighter nuclei with fragmentation and condensation).

3. I suggest studying with deep detail the apoptotic results. This is a very critical point, then morphologic characterization (as previously mentioned) and study of the role of caspases in this model is crucial.

Response: For your helpful advices, we rewrite the paper and showed the DAPI stain of the apoptotic nuclear and cytoplasmic changes. The T-2 toxin as an environmental factor in this model is crucial, however, we have run out of T-2 toxin recently, so we will discuss the influence of T-2 toxin together with our original nano-selenium on the chondrocytes apoptosis in later experiments.