Author's response to reviews

Title: The expression of Gli3, regulated by HOXD13, may play a role in idiopathic congenital talipes equinovarus

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Author's response to reviews: see over
Dear Dr. Rikki Graham,

Thank you for your kind letter regarding manuscript (No. 4772673862723102) dated 10.1.2009, and the referees’ remarks. We are happy to know that our paper will be acceptable. We have revised and modified the MS in accordance with the reviewers’ comments. At this time, we have re-submitted the revised MS and we hope to have an opportunity to publish this paper in your journal.

Below, please find our responses to the revisions proposed by the reviewers’ comments.

**Reviewer #1:**

1. *The animal model is still troubling. I realize there is not a good animal model for but it is not clear what conclusions can be made by performing studies on the chosen model. This is a significant limitation to what the authors can conclude and is a flaw in the study design.*

Response: We thank the reviewer for pointing this out. We acknowledge the limitations of our animal model induced by all-trans-retinoic acid, but up to now, there is not a good animal model for clubfoot. In this study, all-trans-retinoic acid induced both clubfoot and other forms of malformations. In order to investigate ICTEV mechanism, we reviewed previous studies (see the references 1-6). They all used retinoic acid to induce clubfoot. In this study, we carefully selected the model animals. Only fetal rats with clubfoot were selected to ensure that the animal model is related to the real patients as closely as possible. From this model, we found the both mRNA and protein expression levels were increased. Elevated Gli3 gene expression might be related to ICTEV.

Suitable animal model is very important for investigating ICTEV. We are searching for a better ICTEV animal model and planning to carry out further research, which has been funded by the National Natural Science Foundation of China (Project No.: 30973140). We have addressed these concerns in the DISCUSSION in the revision including the limitations of this model.

References


2. In general, the authors need to temper their conclusions to match only what was reported in the results section. The conclusion section, in other words, should more closely follow what results were reported.

Response:
Thank you for your suggestions. We carefully reviewed our data in this study, and made conclusion from our findings. We made the revision in Conclusion section.

Reviewer #3:

I would ask the authors to substitute Fig2C because it is out of focus and the malformation is not appreciated. A higher magnification, even if focusing only in the hindlimbs, would be most useful.

Response:
We have made revision as you suggested.
I believe the manuscript has been improved satisfactorily and hope it will be accepted for publication in *BMC Musculoskelet Disord*.

Best regard

Sincerely yours,

DongHua Cao