Author's response to reviews

Title: Establishment of the mild, moderate and severe dry eye models using three methods in rabbits

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Author's response to reviews: see over
Dear Editors and Reviewers,

Thanks very much for your letter and for the reviewers’ comments concerning our manuscript entitled “Establishment of the mild, moderate and severe dry eye models using three methods in rabbits” (MS: 7413399989308625). We have studied the comments carefully and have made correction which we hope meet with approval. The main corrections in the paper and the responds to the reviewers’ comments are as flowing:

Response to reviewer Prof. Chuanqing Ding:

1. Response to comments: In most cases within the text, “Significant higher/lower/etc…” should be replaced with “Significantly…”

   Thanks for your advice, and we have corrected these grammatical mistakes.

2. Response to comments: anesthesia methods should be moved from 2.2 to 2.1.

   We have moved that from 2.2 to 2.1.

3. Response to comments: The texts in figures were not clear, although figures themselves appear ok.

   Thanks for your advice. Indeed, our most pictures were performed by Statistical Package for Social Science (SPSS), and our former
papers, whose figures were performed the same way, were published in SCI journals (for example: Protective effects and mechanism of tetramethylpyrazine against lens opacification induced by sodium selenite in rats, Exp Eye Res, 2011; Comparison of the Schirmer I test with and without topical anesthesia for diagnosing dry eye, Int J Ophthalmol, 2012). In spite of this, we tried our best to optimize these images to make them clear not only of figures themselves but also the texts in figures.

4. Response to comments: References should be double checked to conform to journal style.

We have checked the references carefully once more to conform to the journal style.

5. Response to comments: Table of abbreviations appear unnecessary, unless they’re required by the journal, as these have been abbreviated in the text

We have removed the table.

6. Response to comments: Figure 7 showed no description of what was presented. It would be helpful to include a scale bar in the figure.

We displayed figure 7 in our paper to compare the characteristics of the two glands, and we have described the details in our paper (part 3.4), so we did not repeat that in the legends. Besides, we have added scale bars to figure 7.
Response to reviewer Prof. Wei Chen:

1. Response to comments: The methods used in this study have already been reported, and they are used to establish severe dry eye models. And the pathogenesis of the dry eye induced by these methods does not accord with that of the major types of human dry eye disease, so these rabbit models are not good choices for current dry eye research. And I also doubt that the method of removing the lacrimal gland, Harderian gland, and nictitating membrane only produces mild dry eye in rabbits.

    First of all, we ensure the authenticity of our experiment, which were results of scientific and systematic design, strict performance, reasonable statistics and hard work, and our conclusions were supported by the data presented. Furthermore, although there were many publications regarding the establishments of DE models, these reports failed to describe details regarding degrees of DE, not to speak of comparison between different DE models. The multi-factorial and multi-mechanism natures of DE clearly warrant further investigation. Therefore, we built three different models, not only with different mechanism but also of different degrees, showing us the important of both lacrimal glands and goblet cells, which increased our understanding to the etiology and pathogenesis of DE, on behalf of the major types of human DE disease.
2. Response to comments: Generally, this manuscript needs the help of someone proficient in English to make it better understood. There are several typos and grammatical errors that need correction.

   Our manuscript had been edited by a medical editor who is a native English speaker associated with MedCom Asia, Inc., and we will attach the certification. Our former articles published in SCI journals were edited by the same company. (for example: Protective effects and mechanism of tetramethylpyrazine against lens opacification induced by sodium selenite in rats, Exp Eye Res, 2011; Comparison of the Schirmer I test with and without topical anesthesia for diagnosing dry eye, Int J Ophthalmol, 2012; The comparative protective effects of Ganoderma spores lipid and fish oil on N-methyl-N-nitrosourea-induced photoreceptor cell lesion in Rats, Evidence-Based Complementary and Alternative Medicine, 2011)

3. Response to comments: In the Abstract, the authors failed to describe the induced dry eye of the three eye groups with clarity. Besides, specific p values are needed rather than general “p<0.05” (also in the manuscript).

   In abstract, we introduced our experiment as simple as possible, and we thought we have clearly summarized the experiment. If we add something, there would be too much, which we thought unnecessary.

4. Response to comments: In the Results, the author should identify the
eyes in comparison rather than “group A, group B and group C”, because the left eyes are experimental eyes while the right eyes are control eyes. Figure 3 is not sound enough for it fails to present the differences of the induced dry eye models among groups. Indeed the left eyes are experimental eyes while the right eyes are control eyes, so we know if the models were successfully built, however, all left eyes between group A, group B and group C are also in comparison with each other, to know the differences between every two kinds of DE models. Figure 3 displayed one of these comparisons.

5. Response to comments: In the Discussion, information in the first paragraph seems to be redundant, and there are too many words repeating those in the Results, which should be avoided as possible.

Dry eye, is a multifactorial disease of the tears, so in the first paragraph of the Discussion, we detailedly stated the composition and source of tear film in rabbits, to lay the ground for succedent analysis. Our results included a number of comparisons, so we broadly presented our results in the discussion part to avoid getting readers in confusion.

6. Response to comments: In addition, it is not a good choice for the authors to choose rabbit to establish dry eye model, because the monoclonal antibodies against rabbit are very limited, which is a disadvantage for further research on dry eye inflammatory factors and
cytokines.

Maybe it is limited if only considering antibodies, but we still think rabbit is a good choice in general. We chose rabbit to establish dry eye model because not only they have large eyes amenable to slit-lamp microscopic examinations, but also they have gentle nature and need relatively low cost to maintain. Furthermore, even if there are limited antibodies, we can choose other further research without monoclonal antibodies.

We appreciate for the warm work of editors and reviewers earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.

Yours sincerely,

Deng Xinguo

July 13, 2013