Author's response to reviews

Title: Protocadherin-1 is a glucocorticoid-responsive critical regulator of airway epithelial barrier function

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

Thank you for your letter dated 2/March/2015. We are pleased to know that our manuscript has been rated as potentially acceptable for publication in *BMC Pulmonary Medicine*, subject to adequate revision and response to the comments raised by the reviewers.

Based on the instructions provided in the decision letter and comments provided by the reviewers, we have revised the manuscript by modifying the relevant sections of the manuscript. We have uploaded a copy of the original manuscript marked with all the changes made during the revision process. The revisions made are shown in tracks. Also appended to this letter are point-by-point responses to the comments raised by the reviewers.

We would like to take this opportunity to express our sincere thanks to the reviewers who identified areas of the manuscript that needed corrections or modification. We would also like to thank you for allowing us to resubmit a revised copy of the manuscript.

We hope that the revised manuscript is accepted for publication in *BMC Pulmonary Medicine*.

Sincerely Yours,

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Response to the reviewers

We wish to express our appreciation to the reviewers for his or her insightful comments, which have helped us significantly improved the paper.

Reviewer #1

With regard to the reviewer’s comment on “There are no differences on the expression levels of PCDH1 between normal mucosa in control and NR in CRS”: in this sentence and the same sentence describing results in asthma, should read "...no differences IN the expression levels..."

Response; we inserted the new sentence “There are no differences in the expression levels of PCDH1 between normal mucosa in control and NR in asthma.” into the result section of the revised manuscript (page 12, line 12-13 in the revised manuscript).

With regard to the reviewer’s comment on "In the present study, we did not study the effect of PCDH1 knockdown on primary cultured epithelial cells, because we could transfect efficiently miRNAs into primary airway epithelial cells and keep it for a certain period. So, it is one of the limitations of our study": this is awkward. As an alternative: "A limitation of our study is that we did not primary cultured airway epithelial cells, because of technical difficulties in achieving sustained siren knock-down in primary cells".

Response; we corrected the sentence according to the reviewer’s suggestion. (page 13, line 20-23 in the revised manuscript)

With regard to the reviewer’s comment on "We used several source of lung section including 2 autopsy samples obtained the fatal asthmatic patients. In common, all patients were relatively severe asthmatic patients with airflow limitation. Recently, pathogenesis of asthma is recognized to be heterogenous and complexities. Although we couldn't clarify how the PCDH1 is involve in the pathophysiology of asthma, we showed that downregulation of PCDH1 would be associated with progression of disease severity of asthma": awkward. Instead: "We used several sources of lung section including autopsy samples obtained from fatal asthmatic patients. All patients were relatively severe asthmatic patients with..."
airflow limitation. In future studies, it will be important to study the expression and function of PCDH1 in larger numbers of subjects with varying asthma severity”.

Response; we corrected the sentence according to the reviewer’s suggestion. (from page14, line 25 to page 15 line 1 in the revised manuscript)

Reviewer’s 2

With regard to the reviewer’s comment on” 1. Lack of use of primary cells: please review the line in the discussion in which this is now discussed and correct it: … we could not transfect efficiently ….. Please also edit the way this is described as a limitation. In general, I suggest that all the new additions to the manuscript should be checked for the appropriate use of English language.

Response; we revised the sentence pointed by the reviewer to “A limitation of our study is that we did not study the effect of PCDH1 knockdown on primary cultured epithelial cells because of technical difficulties in achieving sustained siRNA delivery into primary cells” in the revised manuscript (page13, line20-23)

With regard to the reviewer’s comment on” Polarity and differentiation. I do not agree with the statement that apical-basal polarity is the most important feature of epithelial differentiation. The cell lines used do not form cilia, goblet cells and club cells. Therefore, these can not be referred to as differentiated cells.

Response; I appreciate the reviewer’s comment. Therefore, we changed the term “polarized” from “differentiation” in the revised manuscript. (page 10, line3; page 13, line2; page13, line9; )

With regard to the reviewer’s comment on” Diagnosis of asthma. If in all patients reversibility and/or airway hyperresponsiveness was assessed (as described in the GINA guidelines), this is correct. However, I do not understand the phrase “but not all”. Does that mean that these data were not obtained in all patients, and that therefore not all met the GINA guidelines? Please clarify.
Response; Asthma was diagnosed on the basis of the global initiative for asthma (GINA) guidelines. All patients in this study met the GINA guidelines.