

Lian-Sheng Ma
President and Company Editor-in-Chief

Dear Dr Ma,

Re: ORMDL3, Rhinovirus and Asthma

Thank you very much for your inviting me to submit a revised manuscript that addressed the reviewers' concerns. I was pleased to learn that the reviewers found that my manuscript was interesting and I appreciate the reviewers for the helpful suggestions and comments that have improved the paper and I have revised the manuscript and answered all of their concerns. Below are my point-by-point responses. The reviewer's comment is given in bold, with my response following after. We have also submitted the revised paper with all changes marked in red.

Reviewer 1:

Q: Any data concerning the phenotype (allergic, eosinophilic, non eosinophilic etc) of asthma related to ORMDL gene polymorphism?

A: The polymorphisms of *ORMDL3* have been found to associate with many asthma or atopy phenotypes including eosinophil counts in blood. The detailed explanation is out of the topic of current review; however I added a sentence in the introduction in the revised manuscript.

Q: ORMDL3 is expressed in eosinophils and some data showed that, In adult subjects, the number of T alleles at SNP rs7216389 ci related to significantly greater FeNO levels and peripheral eosinophil counts (Schwantes EA et al J Asthma Allergy 2017).

A: I added this reference in the manuscript accordingly.

Reviewer 2

Q: Please cite table 1 on the text. Importantly, the author highlights the potential investigation methods and applications. The quality of the manuscript is very good, with few typos.

A: I added a sentence for the citing Table 1 in the text. Many thanks for the Reviewer's encouragement. The whole manuscript was checked for the typos.

Q: I would suggest changing the title to remove the "asthma".

A: Thanks for the suggestion. Indeed, I do not talk much about asthma in the manuscript, but the whole manuscript explains the role of ORM DL3 in the human rhinovirus infection, the infection causes asthma in childhood and the potential mechanisms are very much relevant to asthma. Therefore, I would prefer to keep the current title.

Thanks for reviewing the manuscript.

Yours sincerely,

A handwritten signature in blue ink, appearing to read 'Y. Zhang'.

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