

Peer Review File

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Reviewer A

The paper titled “Store-operated calcium entry enhances the polarization and chemotaxis of neutrophils in the peripheral venous blood of patients with bronchial asthma by upregulating ERM protein” is interesting. The polarization and chemotaxis of neutrophils in the venous blood of patients with asthma are increased. This may be due to the abnormal expression and distribution of ERM and F-actin as a result of abnormal SOCE function. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) The abstract is not sufficient and needs further modification. The research background did not indicate the clinical needs of the research focus.

Reply 1: I have modified it in the part of abstract, Line 56-61.

2) What are the cell intrinsic mechanisms that regulate neutrophil polarization and chemotaxis? How does the relationship among regulatory mechanisms change when cells change their direction of migration? It is recommended to add relevant content.

Reply 2: I have modified it in the part of introduction, Line 163-172.

3) What is the pathogenesis of SOCE involved in airway inflammation and remodeling in bronchial asthma? It is recommended to add relevant content.

Reply 3: I have modified it in the part of introduction, Line 186-197.

4) There have been many studies on bronchial asthma. What is the difference between this study and previous studies? What is the innovation? These need to be described in the introduction.

Reply 4: I have modified it in the part of introduction, Line 198-204.

5) Figure 6 are not clear enough. It is recommended to provide clearer figure again.

Reply 5: I have replaced a Figure with 43Mb in the manuscripts.

6) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “The role of inducible costimulatory molecular ligand (ICOSL) in children with neutrophilic asthma, *Transl Pediatr*, PMID: 32953544”. It is recommended to quote the articles.

Reply 6: I have modified it in the part of introduction, Line 119-124.

7) What is the role of neutrophils with different functional polarization in the asthma response?

It is recommended to add relevant content.

Reply 7: I have modified it in the part of introduction, Line 127-134.

Reviewer B

1. Figure 1

a) Please provide the staining method in the legend if applicable.

b) Please provide the observational method in the legend for figure 1A, 1C, 1E, 1G.

I have revised and there was no staining method and we just observed the neutrophils under microscope.

2. Figure 2

a) Please provide the staining method in the legend.

b) Please provide the scale bar in the figure or magnification in the legend.

c) As there is no symbol “*” in the figure, please delete the explanation in the legend.

neutrophil migration and corresponding chemotactic potential statistical figure.

Compared with the *t* test, * $P < 0.05$ and ** $P < 0.01$ vs. the healthy control group. HC, healthy control; fMLP, N-formyl-methionine-leucine-phenylalanine; IL-8, Interleukin

I have revised.

3. Figure 3

There's no scale bar in the figure, please provide. Besides, it's “scale” not “scar”.

min at 37 °C. Cells were fixed and stained with rhodamine-conjugated phalloidin. Scar bars represent 5 μm. HC, healthy control; fMLP, N-formyl-methionine-leucine-

I have revised.

4. Figure 4

a) Please explain the meaning of the green arrows in the legend.

b) There's no scale bar in the figure, please provide. Besides, it's “scale” not “scar”.

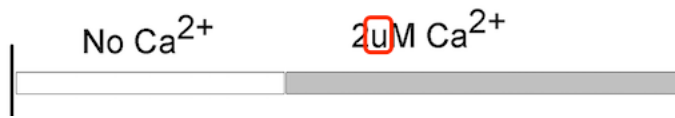
37 °C. Cells were fixed and stained with rhodamine-conjugated ERM. Scar bars represent 5 μm. HC, healthy control; fMLP, N-formyl-methionine-leucine-phenylalanine; IL-8, Interleukin-8; DAPI, 4',6-diamidino-2-phenylindole; DIC,

I have revised.

5. Figure 6

Here should be μ, please revise.

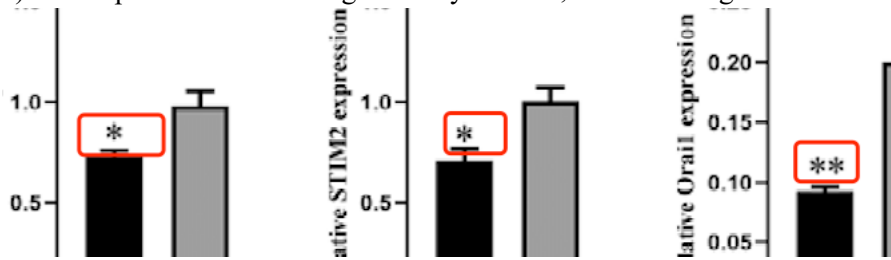
A



I have revised.

6. Figure 7

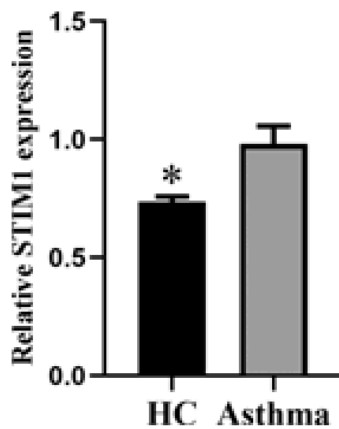
a) Please provide the meaning of the symbol “*, **” in the legend.



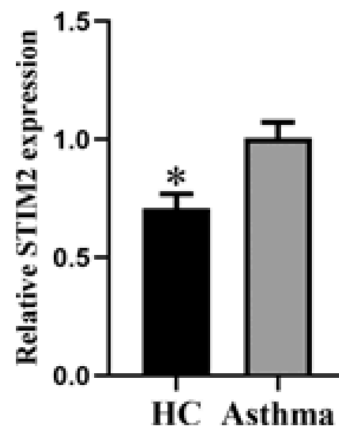
I have revised.

b) Please provide a clearer version of figure 1, the current one cannot be seen clearly (as you can see the screenshot below).

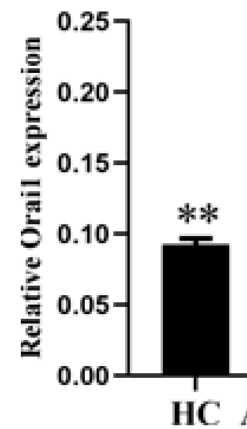
B



C



D



I have revised.

7. References/Citations

Please double-check if more studies should be cited as you mentioned “studies”. OR use “study” rather than “studies”.

According to an inflammatory phenotype classification(57), allergic asthma belongs to the “eosinophilic phenotype.” Notably, while patients with more than 3% sputum eosinophils are considered eosinophilic, up to 60% sputum neutrophils can be present(56-58). **Studies** that have examined the role of eosinophils in allergic asthma pathogenesis have underscored a potential proinflammatory, deleterious effect that facilitates type 2–mediated disease development(59).

I have revised.