We thank the editors and reviewers for your careful consideration of our manuscript # 74452, entitled " Effects of Glucocorticoids on Leukocyte: genomic and non-genomic mechanisms". We have carefully considered all the comments and made modifications to the manuscript specifically indicating what was done in our point by point response to the reviewers listed below.

- 1. We have revised references 7 and 45.
- 2. We have supplemented the citation locations for Figure 1 and Figure 2.
- 3. We have provided the Figures cited in the original manuscript in the form of PPT.
- 4. We have added some suggestions for further clinical approach in the conclusion.
- 5. We have sent the revised manuscript to a professional English language editing company again.

ROUND 2

For the second-round review, we have revised the manuscript according to its comments and made a point-to-point response to the review comments.

Author made clearer information in the manuscript. However in the conclusion it remains unclear suggestion for further clinical approach based on the findings

We have added some suggestions for further clinical approach in the conclusion.

ROUND 1

For the first round of review report, we have replied point-to-point to each reviewer's comments:

Reviewers' comments:

the purpose in this study was unclear and lack of novelty. discussion only
paraphrase other studies. in the conclusion it said "Clinically, the effects of
GCs on white blood cells are similar to the effects of bacterial infections on
white blood cells, which may lead to the overuse of antibiotics". Based on
basic and clinical pharmacology, GC can not be used in infection due to its
immunosuppressant effect. Please referee this study to the pharmacology
theory.

We agree your opinions that GC can't be used in infection due to its immunosuppressant effect. The sentence in my manuscript is mainly directed at patients requiring glucocorticoid treatment, such as nephrotic syndrome, systemic lupus erythematosus, sjogren's syndrome and other diseases. During glucocorticoid treatment, white blood cells will increase, which is similar to the change of white blood cells in infection. Some doctors may misunderstand patients suffer with infection and may lead to the overuse of antibiotics. And we have amended this sentence to make them easier understand.

2. 1 Title. Appropriate 2 Abstract. Appropriate 3 Key words. Keywords should contain words different from the title, this can attract more audiences during search. 4 Background. Since the manuscript is not a meta analysis; the method for the selection of the included articles should be omitted, or it should be rewritten in a manner containing more detail about the selection/inclusion way 5 Methods. Not relevant 6 Results. Not relevant 7

Discussion. The presented information is new and interesting. The flow of the article is easy to follow and understand. The manuscript can attract attention and citation. 8 Illustrations and tables. The main conclusions can be summarized in a brief table. 9 Biostatistics. Not relevant 10 Units. Not relevant 11 References. Appropriate 12 Quality of manuscript organization and presentation. Appropriate 13 Research methods and reporting. Not relevant? 14 Ethics statements. Not relevant.

We have removed the method for the selection of the included articles and changed keywords. And we have added two figures to summarize the effects of glucocorticoids on leukocyte (figure 1) and the mechanism of glucocorticoid action (figure 2).

3. <u>Please provide a figure - like a graphical abstract or GC mechanism of</u> actions highlighting your results compared to traditional point of view

We have added two figures to summarize the effects of glucocorticoids on leukocyte (figure 1) and the mechanism of glucocorticoid action (figure 2).

4. The study is aimed to summarizes the relevant research on the effects of glucocorticoids on leukocytes in recent decades. The title is Effects of Glucocorticoids on Leukocyte: genomic and non-genomic mechanisms . 1. Several factors influence the effects of glucocorticoids. Please discuss these. 2. Please also summarize in the form of Table . 3. What is the new knowledge of the report? 4. Please recommend to the readers How to apply this knowledge? .

1. The role of glucocorticoids is mainly dependent on glucocorticoid receptors, so the function of GCs is significantly affected by the number of GRs. 2. We have added two figures to summarize the effects of glucocorticoids on leukocyte (figure 1) and the mechanism of glucocorticoid action (figure 2). 3. We made a point that the effects of GCs on leukocytes were similar to the change in peripheral blood caused by bacterial infections. Thus, it is necessary to be vigilant in clinical activity to avoid excessive use of antibiotics. The mechanisms of GCs function have not clear, and further research on these mechanisms will help to develop new therapeutic strategies.