

Ms. No.:26964

**The role of A20 in inhibits lipopolysaccharide-induced inflammation in enterocytes**

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Dear Editor,

*World Journal of Gastrointestinal Pharmacology and Therapeutics*

I acknowledge receipt of your letter regarding the above-captioned manuscript. We appreciate the constructive comments made by the reviewers, and I have made a point-to-point response to the reviewer's comments, as per attached.

Yours truly,

Ying Huang

July 11, 2016

## **Reviewer 1**

### **Question 1**

Keywords: Why did authors chose TNF-alpha? in paper you also concentrate on IL-8 and IL-1. Results: page 3, 13, analysis of IL-6 is described in the paper. I did not found the results for this interleukin.

### **Answer**

Thanks very much for your beneficial suggestion. I think you are right. Although TNF-alpha was mentioned many times in the manuscript, but it was only a part of the results, so as a keyword, maybe it is not suitable. The keyword "TNF-alpha" was deleted in the revised manuscript. Please see page 4, line 5.

### **Question 2**

Page 7: There is no the whole name for the shortcut "IEC"

### **Answer**

Thanks very much for your kind reminder. The whole name for shortcut "IECs" has been given out in page 6. To maintain consistency, I think "IECs" is more suitable. . Please see page 7, line 10 (in blue).

### **Question 3**

Page 7: Escherichia coli should be in italics. Please add B in the brackets (Figure 2B and 3B) Page 10

### **Answer**

Thank you for your beneficial suggestion. I have modified it. Please see page 7, line 19 and page 10, line 10 and 11 (in blue).

### **Question 4**

Section: Overexpression...I suppose there are mistakes in the numbers of Figures: there should be Figure 4 and 5 Page 12

### **Answer**

First, we want to apologize for the mistakes, and thank you very much for your kind reminder. There are indeed some mistakes in the numbers of Figures. We have

modified it in the revised manuscript. Please see page 10, line22 and 26 (in blue).

### **Question 5**

Page 12: for IBD is always needed, "always" sound not good.

### **Answer**

Thank you for your suggestion. The word "always" is deleted in the revised manuscript. . Please see page 12, line 4 (in blue).

### **Reviewer2**

### **Question 1**

In Fig. 4, it is not clear what was tested. Did overexpression of A20 decrease nuclear translocation of the p65 subunit? Or phosphorylation of I $\kappa$ B $\alpha$ ? Or ubiquitination of I $\kappa$ B $\alpha$ ? The authors only wrote NF- $\kappa$ B and this is quite unclear.

### **Answer**

As showed in the manuscript, overexpression of A20 decreased nuclear translocation of the p65 subunit. We want apologize for not writing it clearly in the figures legend. We have complemented this information in the revised manuscript. Please see page 10, line 22, 24 and 26; and page 23 and 24 (in blue).

### **Question 2**

In the Fig. 6 legend, the authors stated that there were no differences among the 3 groups. However, statistical significance (\*) was indicated at certain time points. This is quite confusing.

### **Answer**

Thank you for your question. I think there may be some misunderstanding for you. As showed in the manuscript figure legend, there was no significant difference in the expression of TNF- $\alpha$  among the control group, A20 knockdown-control group and A20 overexpression-control group, but the statistical significance (\*) was showed among control group, A20 knockdown group and A20 overexpression group.

### **Question 3**

In Figure 7, panels were labeled 1 to 4. Letters A to D should be used instead of numbers so that all Figures are consistent.

**Answer**

Thank you very much for your kind advice. As showed in the manuscript figure legend, A, A', B and B' represent for different cell groups. If the panes were labeled as A to D, I think there may be some confusion, so panels were labeled 1 to 4 instead.

**Reviewers 3**

**Question 1**

My only concern is related to the introduction section. At the final of the introduction the aim of the study is not clearly defined. The last paragraph of the introduction presents some conclusions that may be deleted and included at the final of the discussion section.

**Answer**

We have added the aim of the study at the final of the introduction, and deleted the conclusions parts at the final of the discussion section in the revised manuscript. Please see page 3, line13 and14 (in blue).

**Changes made in the manuscript as discussed above are shown in blue to enable easy detection during the review process.**