

Reviewer 3

Questions and Answer:

The authors have significantly modified the manuscript and answered most of related queries. However there are some minor corrections that need to be addressed before publication.

Reply: We thank for your suggestion. We have revised some spells and done language editing in our manuscript by Professional English Language Editing Services (WRITE SCIENCE RIGHT, USA).

1. Figure 1: the authors should include $**p < 0.01$ in the figure legend. In the result section (3.1) the authors mentioned use of 10 μM and 20 μM 4-MU doses, while the figure denotes 20 μM and 40 μM . The authors should check it.

Reply: Thanks for your reminding. We have revised the mistake. 20 μM and 40 μM doses is correct.

2. Figure 5: The authors should remove $*p < 0.05$ and include $***p < 0.001$ in figure legend.

Reply: Thanks for your reminding. OK.

3. Supplemental Figure 1: Figure legend is missing.

Reply: In fact, the Figure legend is in our manuscript (doc or pdf). In the manuscript (LaTeX) developed by submission platform, Figure legend is missing. We have add it to the revised manuscript again.

4. Method (Western blotting): The authors should include Ab for p65, p-p65, I κ Ba and GAPDH and also mention how the data was analyzed. The phosphorylation sites of all Abs used should be mentioned.

Reply: We have revised them. Thanks for your constructive suggestion.

Our revised manuscript:

“Rabbit monoclonal IgG primary antibodies against JNK (c-Jun N-terminal kinase), phosphorylated (p)-JNK (Thr183/Tyr185), p-SYK (spleen tyrosine kinase, Tyr525/Tyr526), ERK (extracellular signal-regulated kinase), p-ERK (Thr202/Tyr204), p38, p-

p38 (Thr180/Tyr182), and anti-GAPDH (glyceraldehyde 3-phosphate dehydrogenase) (Cell Signaling Technology, Danvers, MA). We bought rabbit monoclonal primary antibodies targeting SYK, p65, and I κ B α from Abcam (Cambridge, MA) and bought IgG κ BP-horse radish peroxidase (HRP), anti-rabbit IgG-HRP, and monoclonal IgG anti-p-p65 (Ser311) primary antibodies from Santa Cruz Biotechnology (Dallas, TX). ”

“The membranes were incubated overnight at 4 °C with anti-SYK [1:1000], anti-p-SYK [1: 1000], anti-ERK [1:1000], anti-p-ERK [1:1000], anti-JNK[1:1000], anti-p-JNK [1: 1000], anti-p38 [1:1000], anti-p-p38 [1:1000], anti-p-p65 [1:200], anti-p65 [1:5000], anti-I κ B α [1:2000] and anti-GAPDH [1:2000] primary antibodies in TBS-T. The membranes were then incubated for 1 h with HRP-conjugated secondary antibodies [1:2000]. Immunoreactive protein bands were visualized by reaction with chemiluminescent reagents (Meilun Biotechnology Co., Ltd (Dalian, China). The relative levels of p-SYK/SYK, p-ERK/ERK, p-JNK/JNK, p-p38/p38, p-p65/p65 and I κ B α /GAPDH were analyzed statistically using Image J software (National Institutes of Health, Bethesda, MD, USA).”

5. The method used to measure the ear thickness should be included.

Reply: Thanks for your reminding. The ear thickness was measured by electronic digital caliper (Deli, Zhejiang, China).