Dear Editor-in-Chief, Ma

Thank you very much for allowing us to revise our manuscript "DKK1/CAKP4 signaling activation by *Helicobacter pylori*-induced AP-1 promotes gastric tumorigenesis via the PI3K/AKT/mTOR pathway", by Jian-Jiang Zhou et al., for publication in "*World journal of gastroenterology*". We also think the reviewer for his constructive comments on the manuscript. We have revised the manuscript based on the reviewer's comments in the revised version. Our point-by-point response to the reviewer's comment is detailed below.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is interesting work; However: 1- Core tip could even be more informative by the current findings within this study. 2- Introduction was to long. 3- Method and results was complete; However, please give more details regarding RNA-seq, Co-immunoprecipitation, as well as Lentivirus infection to be repeatable by readers.

Response: Thank you for your good suggestion. In the revised version, we have revised the Core tip section and incorporated more findings from this study (P_4). We have also shortened the introduction (P_{4-5}) and give more details to the readers about RNA-seq (P_7), co-immunoprecipitation (P_{10}), and lentivirus infection experiments (P_{11}) in the Method section.

4- The quality of figures is low, please use high quality images.

Response: Thank you for your observation. We have uploaded the high-quality electronic version of the figures.

5- Discuss about study limitations.

Response: Thank you for suggestion. We have added the contents to the discussion section of the revised manuscript (P_{18}).

There were several limitations to this study. First, the number of clinical samples was small. Therefore, further study with larger sample sizes is

required to determine the expression of the DKK1/CAKP4 axis in GC tissues and its association with *H. pylori* infection in cancer tissues. Second, only two strains of *H. pylori* were used in this study: an East Asian strain (*H. pylori* GZ7) and a western strain (*H. pylori* 26695). However, *H. pylori* exhibit intrastrain and interstrain heterogeneity. More *H. pylori* strains will be required to verify our findings.

6- Conclusion should be objective with further perspective for future investigations.

Response: Thank you for your comment. We have revised it and added new information about future investigations (P_{19}).

The identification of small compounds and drugs targeting the DKK1/CKAP4 axis will be a crucial aspect of future studies. We will also investigate this possibility further.

Reviewer #2:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: The manuscript is well, concisely and coherently organized and presented，but I still have one question： What are the key problems in this field that this study has solved?

Response: Thank you for your question.

Gastric cancer (GC) is one of the most common malignant tumors with a high morbidity and mortality rate globally, especially in East Asian countries. *Helicobacter pylori* (*H. pylori*) infection is the most significant risk factor for GC. Although substantial efforts have been done to link *H. pylori* infection and GC over the past decades, the molecular mechanisms of *H. pylori*-induced GC are not fully understood,

which results in reduced treatment benefits. The present study revealed that *H. pylori*-induced AP-1 promotes the binding of DKK1 to CAKP4, which contributes to gastric tumorigenesis via the PI3K/AKT/mTOR pathway. The findings suggest that the DKK1/CKAP4 interaction may be a therapeutic target for *H. pylori*-induced GC. The identification of small compounds and drugs targeting the DKK1/CKAP4 axis will be a crucial aspect of future studies. We will also investigate this possibility further.

This has been added to the article highlight section on page 19.