

Dear Reviewers:

Thank you for taking the time to review “Cancerous inhibitor of protein phosphatase 2A enhances chemoresistance of gastric cancer cells to oxaliplatin” (manuscript number: 79831). We appreciate your thorough review and critical analysis of our paper. Please see below for our point-by-point responses to the reviewers’ questions.

A1. In the abstract - method chapter I will like to have the volume of the study. This manuscript is interesting us a manuscript which determinate the new approach in oncology and it is personalized therapy. This type of therapy is good because it does not expose patients to unnecessary damage from ineffective chemotherapy. Congratulation.

Answer: We have modified it in response to the reviewer’s comments.

A2. This pathway is difficult for journal readers. Add some schemas for possible pathways. Signaling pathway is important for your conclusion.

Answer: Thank you for your thorough review. After reviewing recent literature, we discovered that the Akt signaling pathway was involved in CIP2A-related drug interactions in a variety of tumors, including lung cancer and breast cancer. Based on this, we designed and conducted this study. Our findings indicated that CIP2A can enhance chemotherapy resistance of gastric cancer cells to oxaliplatin, and that the Akt signaling pathway was involved in this process, which was consistent with previous literature. However, our research group is still investigating the specific target genes of the Akt signaling pathway and its molecular mechanism, which will be reported once the mechanism is fully clarified. As a result, we now only present existing experimental results in the manuscript, and we further interpret our current research results in the manuscript discussion section, combining with relevant literature, to ensure that our research findings are easily understood and accepted by the readers.

References:

1. Luque M, Cristóbal I, Sanz-Álvarez M, Santos A, Zazo S, Eroles P, Arpi O, Rovira A, Albanell J, Madoz-Gúrpide J, García-Foncillas J, Rojo F. CIP2A as a Key Regulator for AKT Phosphorylation Has Partial Impact Determining Clinical Outcome in Breast Cancer. *J Clin Med*. 2022 Mar 14;11(6):1610.
2. FENG Fei-Fei, CHENG Peng, SUN Chao, WANG Hui, WANG Wei. Inhibitory effects of polyphyllins I and VII on human cisplatin-resistant NSCLC via p53 upregulation and CIP2A/AKT/mTOR signaling axis inhibition [J]. *Chin J Nat Med*, 2019, 17(10): 768-777.

A3. The proposed work is very interesting. In fact, it directs towards new and

personalized oncological therapies, which will be able to avoid other useless therapies with side effects. All paragraphs are relevant to the topic; are clearly developed and described. The discussion is suitably broad. Sufficient and clear tables and figures. Updated bibliography.

Answer: We have modified it in response to the reviewer's comments.

Thank you for the guidance provided by the professor.

Sincerely

Yongxun-Zhao