

Dear Editor

Thank you for considering the manuscript entitled "Clinicopathological features and Expression of regulatory mechanism of the Wnt signaling pathway in colorectal sessile serrated adenomas/polyps with different syndrome types" (81721). We really appreciate all the valuable comments and constructive suggestions from reviewers. We have revised the manuscript and a point-by-point response was enclosed. We would like to re-submit the revised manuscript to the World Journal of Clinical Cases, and hope it is acceptable for publication in the journal. Please do not hesitate to contact us for any question or concern.

We look forward to your final decision.

Sincerely yours

Yan-Cheng Dai

Responses to reviewer:

**Reviewer #1:** The authors indicated that the SSA/P patients with damp-heat syndrome have more Wnt signalling pathway activation which pointed out the higher risk of carcinogenesis. The paper is generally well written and structured. However, some minor issues listed below need to be addressed by the authors. Last sentence of the first paragraph of the introduction "Reportedly, the mortality of proximal colon cancer has decreased, despite the popularity of colonoscopy, which might be associated with the insufficient understanding of SSAs/Ps by endoscopists and the missed diagnosis of SSAs/Ps in the proximal colon [5]." is a little bit confusing. Authors are requested to check this sentence again. "Immunohistochemical analysis and criterion for judgement" title should be replaced with "Immunohistochemical analysis" Authors are asked to have any observation between size/location clinical features and b-catenin, APC, MCC staining in Patients with damp-heat syndrome. Authors are requested to share their findings in systemic and more detail. Results section shouldn't be presented in an

ordinary way. Authors are recommended to explain the association with the hypothesis of the findings in the “Case source and baseline data comparison” part of the Results section. Group names should be indicated in Figure 3 and 4. Left panels of the figures can be used for the labeling.

**Response:** We have revised the manuscript. Last sentence of the first paragraph of the introduction “Reportedly, the mortality of proximal colon cancer has decreased, despite the popularity of colonoscopy, which might be associated with the insufficient understanding of SSAs/Ps by endoscopists and the missed diagnosis of SSAs/Ps in the proximal colon [5].” was confusing, and we revised it. From baseline data comparison, significant differences in the SSA/P size between the two groups of patients with different syndrome types were observed, while no differences were observed in terms of the other aspects. Therefore, Pearson analysis was performed for the correlation between the SSAs/Ps size and protein expression of  $\beta$ -catenin, APC, and MCC in each group. We added Figure 5. Group names were indicated in Figure 3 and 4.

Thank you for your valuable advice.

**Reviewer #2:** Nice study on expression of Wnt signaling pathways in serrated polyps and its role in colorectal cancer. Some of the comments' are as follows:  
1. Titles needs modification as " Clinicopathological features and Expression of regulatory mechanism of the Wnt signaling pathway in colorectal sessile serrated adenomas/polyps with different syndrome types"  
2. Addition of a table with differentiating clinical features, pathological features and IHC finding comparing both the syndromes would be better.  
3. The paragraph " -----and treatment, traditional Chinese medicine treatment based on syndrome differentiation, and regular follow-up were essential" must be deleted from the conclusions - both from the abstract body and also from the

main manuscript, because this study does not involve the study on the Traditional Chinese Medicine (TCM) 4. Language and grammar needs significant polishing.

**Response:** We have revised the manuscript. We have revised the title of the article to " Clinicopathological features and expression of regulatory mechanism of the Wnt signaling pathway in colorectal sessile serrated adenomas/polyps with different syndrome types ". The clinical features of SSAs/Ps with different syndrome types are shown in Table 1. There are similarities of the pathological features of SSAs/Ps according to pathological diagnostic criteria, and we added these contents in the first paragraph of the discussion section. The IHC findings are shown in Table 2. We deleted the paragraph from the abstract body and also from the main manuscript. The language and grammar problems in the manuscript have been refined again. Thank you for your valuable advice.