

Reviewer 1

This is an interesting study about the clinical value evaluation of serum markers for early diagnosis of CRC. As cancer increases, CRC shows changes in bowel habits, blood in the stool, diarrhea, alternating diarrhea or constipation, local abdominal pain and other symptoms. In the advanced stage CRC, it shows anemia and body weight loss or other systemic symptoms. A typical CRC is developed from a focal change in benign, precancerous polyps. These polyps are local growths or the accumulation of abnormal cells in the intestinal mucosa that protrude into the intestinal lumen. Clinical screening for colorectal cancer involves colonoscopy, sigmoidoscopy and CT. Screening for biomarkers including CEA, CTC, circulating tumor DNA/RNA and abnormal DNA methylation. Early screening for CRC plays an important role in combating and controlling the growth of CRC morbidity and mortality worldwide. However, the currently available screening methods are severely inadequate because of their high cost and cumbersome preparation procedures that ultimately result in a low participation rate. Blood-based screening experiments attract the public because of their noninvasive and low patient harm features. This screening is easy to perform and can be repeated in shorter time intervals, which in turn leads to higher participation rates. In this study, the authors analysis multiple methods combined detection used to determine the tumor marker diagnostic value for detection of CRC. The design of the study is very well, results are interesting. The discussion is somewhat long, please shorten it. Table require a minor editing. Figures are good. Some minor language polishing should be corrected, such as "We aimed to to develop a new examination", the second "to" should be deleted.

#### **Answer**

Thanks for the reviewer' comments. We have short the Discussion section. The table had been edited. In addition, the language in the manuscript had also been corrected.



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## **Reviewer 2**

### **SPECIFIC COMMENTS TO AUTHORS**

In this study, Song et al aimed to develop a new examination method based on the serum biomarker panel for the early detection of CRC. The methods of the study is good, and sample size is big. The results are well discussed with update references. The manuscript requires a minor editing before final publication. Some minor language polishing in the abstract and main text should be corrected, this may be due to carelessness in typewriting.

### **Answer**

Thanks for the reviewer' positive comments. The manuscript have been carefully checked, and the language have also been carefully corrected.

**Reviewer 3****SPECIFIC COMMENTS TO AUTHORS**

Interesting study. Minor revision is required. 1. Abstract. "We aimed to to develop a new", please delete the repeated "to"; some "colorectal cancer" should be changed to "CRC". 2. Core tip. "earyl" should be "early". 3. Main text. Also, some "colorectal cancer" should be changed to "CRC". And some blanks are missing, please check it. 4. Tables are good, a minor editing is required. Over all, I recommend to accept the manuscript after this minor revision.

**Answer**

Thanks for the reviewer' careful review. We are very sorry for the wrong description. The question 1 to 4 have been checked and corrected.