

Ze-Mao Gong  
***World Journal of Gastroenterology***

Dear Dr. Gong,

We thank you and the reviewers for the thorough evaluation of our manuscript and the thoughtful comments. In response to the reviewers' comments, we are submitting a revised manuscript entitled "The genomic diversity of colorectal cancer: changing landscape and emerging targets." We have made appropriate edits to the manuscript, which are highlighted, and address each comment point by point as below in bold.

With kind regards,

Tanios Bekaii-Saab  
Professor of Medicine  
Mayo Clinic

**Specific points to address**

Reviewer #1 (Comments to the Author (Required)):

This is a nice and timely review on the most recent evolutions in the field of targeted treatment of colorectal cancer based on the genomic landscape of the disease. The review provides an interesting overview of the current clinical trials and investigational drugs in CRC and I think it would be of interest for the readers of WJG. I have just some minor comments/suggestions. 1. Preliminary data of a possible re-sensitization to anti-EGFR monoclonal antibodies of RAS mutated tumors after a wash out period with other targeted drugs have been recently published and could be of interest for the readers (Siravegna et al, NatCommun, 2015)

**We agree, and this has been addressed in the text of the manuscript**

2. A brief overview of the main TCGA findings for colorectal cancer should be provided

**Further detail of the genomic alterations identified from the TCGA has been added in the paper.**

3. For ctDNA it should be pointed out that although the test sensitivity was low with traditional detection methods ('false negative results' according to the authors), the most recent use of high sensitivity techniques as digital PCR increased to more than 90% the concordance between tumor and plasma DNA

analysis. In addition the analysis of ctDNA in plasma instead of tumor DNA could has the advantage to overcome the problem of tumor genomic heterogeneity.

**We agree with the reviewer and have clarified this in the text.**

4. The source of clinical trial numbers should be mentioned

**The source of the clinical trial numbers has been added to the manuscript.**

Reviewers #2 and #3. No issues have been brought up that require any necessary edits in the paper.