

Professor Ying Dou  
Science Editor, Editorial Office  
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*World Journal of Gastrointestinal Oncology*

Dear Professor Ying Dou,

Manuscript: 47457

“Precision medicine for gastrointestinal cancer: Recent progress and future perspective”,  
by Tasuku Matsuoka and Masakazu Yashiro

As per invitation by the Editor, please find attached a revised version of the original version of our manuscript previously entitled “Precision medicine for gastrointestinal cancer: Recent progress and future perspective”, for which the resubmission fee has been waived.

We are most grateful to you and the reviewers for the helpful comments and have addressed each concern with either new data or modification of the manuscript text. A brief overview of changes made has been included below, and we hope that the explanations and revision of our work is satisfactory.

In writing this paper, English grammar was carefully checked again by Dr. Masakazu Yashiro.

In addition to a number of editorial corrections, the following significant changes (highlighted in yellow) were made to the manuscript.

I would like to change the corresponding author to Dr. Yashiro, because he is more suitable for receiving all correspondence pertaining to the manuscript and responding to requests to edit or submit revisions to the manuscript. We also want to reword the name of our institute, because it has changed recently.

Thank you for your kind attention.

Best regards.

Sincerely yours

Tasuku Matsuoka, M.D., Ph. D.

## Reviewers' comments to the authors

### Reviewer #1:

I commend the authors for realizing significant trends toward more precise diagnosis and treatment of gastrointestinal malignancy. This is certainly the likely path for practitioners in this field. However the authors must make it clear we are in the very very early phases of this transition toward precision and personalized medicine. It is likely that few of the mentioned targeted tools or treatment markers will be utilized a decade from now. Most of the manuscript is very well written. I do take exception to several points however. The sentence "Ineffective drugs can cause progression of cancer without producing any benefit" is patently wrong. Also, colorectal cancer-at least in my experience- has been significantly impacted by the use of colonoscopy as a screening modality. In addition, even patients with widespread CRC may entertain long-term survival and even occasional cure. Gastrointestinal lymphoma such as MALT may also be associated with good response and prolonged survival. In terms of content, perhaps the authors should cover organoids where a patient's tumor is analyzed for both personal treatment and research in the field. In sum, this is an excellent choice of topic and the authors did a reasonable job in covering this broad and complex field. I would just temper some of the statements made.

*Response: We appreciate the reviewer's comments. We added the sentence "At present, we are in the very early phases of this transition towards precision and personalized medicine." in the end of Discussion section. We reword the sentence "Ineffective drugs can cause progression of cancer without producing any benefit" to "The use of inappropriate medicine may not only do not benefit, but lead to cancer progression". We also added the sentences "With respect to CRC, screening has been impacted by the use of colonoscopy as the gold standard, mainly because of its high sensitivity and specificity for detecting cancerous and precancerous lesions. Despite its strengths, colonoscopy has certain disadvantages and limitations (e.g., bowel preparation, sedation, aspiration, perforation, and splenic injury).Therefore, continued progress in novel assays, such as fecal immunochemical test, fecal DNA and other molecular markers, can be expected to further displace screening colonoscopy." on page 9 and 10 of the revised manuscript. We also reword the sentence ".Gastrointestinal (GI) cancer has high tumor incidence and mortality rate in the world and has poor prognosis, which is affected by geographical environment, diet habits and sex" to "Gastrointestinal (GI) cancer has high tumor*

*incidence and mortality rate in the world and has poor prognosis. Although CRC could be largely managed, which results in long-term survival by a combination of drugs even in patients with widespread stage and gastrointestinal lymphoma such as MALT may also be associated with good response and prolonged survival, the overall prognosis of patients with advanced gastrointestinal cancer remains poor.” on page 4 of the revised manuscript. As the reviewer mentioned, we covered GI cancer organoids in Discussion section.*

**Reviewer #2:**

The review has provided an extensive search of the literature on genomic aberrations identified in patients with GI cancer. reported Biomarkers from biological fluids including: blood, urine, seum, plasma, pleural effusion and CSF were summarized in 3 tables. This review may be of clinical value in future if more data are collected, as it will possibly identify biomarkers of prognostic, cost effective and therapeutic predictive value in Patients with GI cancer. The write up as far as language is very good but going through it was not easy possibly because of the many biomarkers and differences between CTCs, ctDNA, MiRNA...etc. the tables as presented were also complicated specially table-1. I am not sure if clinical implication may be presented a, long with targets in a separate table. Alternatively separate table for CTSC, miRNA. Table 2 under publication PMID it is better to be consistent including only PMID number as in table 1 and 3. why listing there the authors? the tables are too crowded. some of the indicators for instance TP53 is common, one can add in the table foot note it is common to all except... Minor typos to be corrected in text and taBLES.

*Response: We appreciate the reviewer’s comments. According to the reviewer’s suggestion, we separate table 1 for CTC, ctDNA, and miRNA, exosome. In table 3, we reword references including only PMID number as in Table 1,2 and 4. We deleted the “Clinical implication” section and simplified the Tables. We have checked he entire manuscript and rewritten carefully to correct English grammar and spelling and to make the manuscript at clear as possible along the reviewer’s recommendation.*