

Point-by-point responses to reviewers' comments

We thank the reviewers for their valuable comments. Our point-by-point responses to these comments are listed below.

Reviewer #1

Li et al. reviewed the recent advances in the diagnosis of gastrointestinal cancer. Although the title is very broad, the text mainly mentions CRC and HCC. Other tumors are mentioned in the text merely.

Response: We thank the reviewer for the comments. We have a preference on CRC and HCC as these are the most common gastroenterological cancers worldwide. We have added the review of recent works on other cancer types (e.g., pancreatic cancer and gastric cancer) in the revised manuscript as suggested.

It is also not clear on the basis of which criteria the authors mentioned some of the articles in the text. There are far more recent studies worldwide.

Response: We thank the reviewer for the comments. In the manuscript, we review the articles that are relatively representative in terms of methodology or biomarkers. In addition, we also have a preference on recently published works (i.e., 2015 to 2020) as shown in Table 1.

There are a far more blood-based biomarkers that have not been mentioned. The authors also often mention liquid biopsy, but focused only on plasma, while the results regarding stool are not mentioned. Overall, the aim of the review is not clear and novelty should be highlighted.

Response: We thank the reviewer for this comment. We have added other blood-based biomarkers (e.g., cell-free RNA) as suggested. We agree with the reviewer there are many fecal-based diagnostic works which are not included in this manuscript. Due to the length limitations and our knowledge in cancer diagnosis, we have focused on blood-based liquid biopsy fields in this manuscript. We have amended the title (“Recent advances in blood-based and AI-enhanced approaches for gastrointestinal cancer diagnosis”) to make the aim of our review clearer as suggested. Our review covers all the common analytes in blood (cfDNA, cfRNA, CTC, and EVs) and 4 major gastrointestinal cancer types (CRC, HCC, PDAC and GC); besides the commonly studied biomarkers, we have spent a high amount of space on cfDNA fragmentomics, which is an emerging direction in cfDNA studies and

less discussed in existing reviews. Hence, we believe that our review could provide valuable knowledge to the field.

Minor:

Figure 1 the text is incorrectly divided in the bubble - extracellular vesicles

Response: We thank the reviewer for the comments. We have fixed this issue in revised Figure 1.

Figure 2 the legend described abbreviations that are not used in the figure

Response: We thank the reviewer for the comments. We have removed the unrelated abbreviations in figure legend as suggested.

Row 222 Exomes – exosomes In the Artificial intelligence-enhanced algorithms

Response: We thank the reviewer for the comments. We have corrected this typo as suggested.

CRC abbreviations shall be used instead of colorectal cancer

Response: We thank the reviewer for the comments. We have widely used the abbreviations in the revised manuscript as suggested.

Reviewer #2

The authors have reviewed good studies for applications of blood-based liquid biopsy and AI-enhanced approaches in gastrointestinal cancers and have submitted a well-written manuscript. It has great value in improving the diagnosis and treatment of gastrointestinal cancers.

1. Comment It will be very helpful to review the sensitivity and specificity of liquid biopsy approaches in the diagnosis of gastrointestinal cancers. In addition, tabulating the given data will be easy to understand.

Response: We thank the reviewer for this comment. We have added a table (Table 1) in the manuscript summarizing the performance (including sensitivity/specificity or the AUC value) of recent works in gastrointestinal cancer diagnosis as suggested.