

## Peer-review

Reviewer #1: 1- it is an interesting topic, but still the sensitivity and specificity did not accurately estimated 2- also, the cost of this molecule is not known 3- large studies are needed to know the exact diagnostic and therapeutic properties of this molecule. 4- the introduction section is long

First of all, thanks for your affirmation of this manuscript. I will reply to your comments as follows.

1- Some of the references included in the manuscript can answer this question. Such as, in reference 51, the authors pointed that “The fluorescence recovery of FAM increases linearly in the 5.0-150 ng·mL<sup>-1</sup> AFP concentration range and has a 1.4 ng·mL<sup>-1</sup> detection limit. The assay was applied to the analysis of spiked diluted human serum. The recovery values ranged from 98.3 to 112.9%, with relative standard deviations of <1.1%”; in reference 53, the authors pointed that “Using this platform, we realized HCC CTCs' capture and identification, the average recovery rate was 61.6% or more at each spiking level. Importantly, our platform identified CTCs (2±2 per 2 mL) in 25 of 42 (59.5%) HCC patients.”; in reference 56, the aptamer-target-antibody construction showed similar performance as conventional ELISA with a detection limit of 62.5 pg/ml; and in reference 60, the HCC-targeting nanoprobe that allowed the successful visualization of orthotopic HCC xenografts with diameters as small as 1-4 mm.

2- We added section 3.1 and reference 49 to the manuscript. This section points out that aptamers are easier and cheaper to produce than antibodies.

3- At present, the application of aptamers in the diagnosis and treatment of liver cancer is still in the stage of continuous exploration. Some of the existing research results have been verified in animal models. We believe that the research on aptamers in liver cancer will be deeper in the near future.

4- We have deleted “ As a type of recognition molecule, aptamers have many advantages, such as high affinity and specificity, a wide range of action, small size, good stability, and easy synthesis and screening compared with traditional immunological and chemical recognition molecules, and aptamers have shown broad application prospects in diagnosis and treatment of disease, including imaging diagnosis, preparation of biological nanomaterials and tumor therapy [6,7].” and “After a rigorously controlled trial, in January 2017, the US FDA approved six oligonucleotides for therapeutic applications. In addition, a variety of drugs are being tested in clinical trials, representing a significant breakthrough in the application of various oligonucleotide drugs, including aptamers [8].” from the introduction of this manuscript.

Reviewer #2: This study focuses on the role of aptamers for the diagnosis and treatment of liver cancer. Introduction may be revised to include the more detailed explanation for aptamers. Please carefully re-check the whole manuscript.

First of all, thanks for your affirmation of this manuscript. I will reply to your comments as follows.

We have added “Now, scientists have acquired a variety of aptamers screened by SELEX technology, which have a special three-dimensional structure that can bind different target molecules [7-8]. The more detailed explanation for aptamers is given below.” on the introduction for this manuscript. The more detailed explanation for aptamers is as follow in section 1.