Dear Dr. Qi, all editors and reviewers:

Thank you very much for giving us an opportunity to revise our manuscript, we would like to express our great appreciation to you and reviewers for your positive and constructive comments on our manuscript entitled "^{125}I-labeled anti-bFGF monoclonal antibody inhibits growth of hepatocellular carcinoma" (ESPS Manuscript NO: 24726).

Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied reviewer's comments carefully and tried our best to revise our manuscript which hope consideration of its possible publication in World Journal of Gastroenterology. All changes in the '24726-Revised manuscript' are highlighted in red.

We greatly appreciate the efficient, professional and rapid processing of our paper by your team. If there is anything else we should do, please do not hesitate to let us know.

Thank you and best regards.

Yours sincerely,

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Responses to the reviewer's comments

1. What success rate have you had with your HCC method?

Response:

Subcutaneous hepatocellular carcinoma (HCC) xenograft model was applied in our present study to test the inhibitory efficacy of ^{125}I-bFGF mAb in mice with HCC. It is characterized by the short modeling period, more easily to manipulate, relatively simple to monitor the size of the tumor and the evaluation of various methods to treat HCC. Mouse hepatoma 22 (H22) is one of the most commonly used mice transplanted tumor cell lines, widely used in mouse HCC animal model. Twenty-five C57BL/6 mice were used to establish the H22 HCC xenograft model, all the mice were successfully formed tumor and the tumor formation rate is 100%.

2. Have you tried the DEN method for HCC genesis?

Response:

DEN method is the chemically DEN-induced hepatocarcinogenesis which characterized by structural DNA changes. Comparative functional genomics showed that the gene expression patterns in HCCs in DEN-induced mouse liver cancers were similar to those of the poorer survival group of human HCCs. We didn't used DEN method for HCC genesis in this experiment, because the average time of DEN method for forming tumor model needed 6 months and the tumor formation rate was low in C57BL/6 mice. According to your good suggestion, we will use DEN method for HCC genesis in our future study of bFGF antibody.

3. On what basis did you decide the dosages?

Response:

We decide the dosages based on the published papers online. In our previous study, the dosage of bFGF mAb for per mouse was 900 μg, once every 3 d in

B16-transplanted melanoma tumors in mice[11]. In addition, we found the dosage of a novel mAb, GAL-F2, specific for FGF2 used in the study was 5 mg/kg body weight, twice per week which was lower than our previous research[18]. Since we labeled ^{125}I with bFGF mAb, so we decreased the dosage of bFGF mAb in our present study, finally the dosage of bFGF mAb for per mouse was 200 μg, once every 3 d.

11 **Zheng SB**, Xu M, Pan LH, Xiang JJ, Deng N, Li D, Wang PP. Synergistic inhibitory effects of bFGF monoclonal antibody combined with radio therapy on B16-transplanted tumors in mice. *Chin J Cancer Biother* 2011; **18**: 175-180

18 **Wang L**, Park H, Chhim S, Ding Y, Jiang W, Queen C, Kim KJ. A novel monoclonal antibody to fibroblast growth factor 2 effectively inhibits growth of hepatocellular carcinoma xenografts. *Mol Cancer Ther* 2012; **11**: 864-872 [PMID: 22351746 DOI: 10.1158/1535-7163.MCT-11-0813]

4. Is the fact that you will look into Bevacizumab relevant?

Response:

Bevacizumab is a potent inhibitor of vascular endothelial growth factor (VEGF) that has demonstrated modest antitumor activity across a broad range of malignancies when combined with chemotherapy[30]. Our experiment showed the increased expression of VEGF in ^{125}I-bFGF mAb treated HCC group. Therefore, we raised the hypotheses when ^{125}I-bFGF mAb combine with VEGF mAb may be conducive to enhance sensitivity to bevacizumab and improve the therapeutic efficacy in the therapy of HCC. By your helpful suggestion to our research plan, we will use ^{125}I-bFGF mAb plus Bevacizumab in treating HCC.

30 **Shah MA**. The development of bevacizumab in noncolorectal gastrointestinal malignancies: gastroesophageal, pancreatic, and hepatocellular carcinoma. *Clin Adv Hematol Oncol* 2014; **12**: 239-246 [PMID:

25003353]

5. Must it be included in the discussion?

Response:

Thank you for your kindly reminding, we really appreciated and totally agree with your constructive suggestion. The sentence "To provide support for this concept, we intend to combine ^{125}I-bFGF mAb and bevacizumab in the treatment of HCC in our future study" is necessary to be included in the discussion, and we have already kept it.

We appreciate for your warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.