Please find the following Response to the comments of reviewers:

Response to Reviewer #1:

Thank you for your elaborate review and the helpful suggestions.

If possible, the authors should add new data regarding MACC1 function or clinical role in gastric cancer.

Response:

Thank you very much. We re-conducted literature search in April 1st, 2016 and found a new publication on MACC1 in gastric cancer and revised the manuscript as follows:

In Page 18: Line 7 to Line 18, we added:

"MACC1 also mediates acetylcholine-induced invasion and migration in gastric cancer. The neurotransmitter acetylcholine (ACh) promotes the growth and metastasis of several cancers via its M3 muscarinic receptor (M3R). ACh acts via M3Rs to promote GC cell invasion and migration as well as expression of several markers of epithelial-mesenchymal transition (EMT). ACh up-regulated MACC1 in GC cells, and MACC1 knockdown using siRNA attenuated the effects of ACh on GC cells. AMP-activated protein kinase (AMPK) served as an intermediate signal between ACh and MACC1. These findings suggest that MACC1 mediates acetylcholine-induced invasion and migration in human gastric cancer cells by participating in the Ach/M3R/AMPK/MACC1 signaling pathway[36]."

Response to Reviewer #2:

Thank you for evaluating our manuscript and for your constructive suggestions.

The manuscript summarizes the current knowledge of MACC1 in gastric cancer. This topic is certainly of scientific as well as of clinical interest. The manuscript is well written and clearly structured. The authors should carefully and sufficiently address the following points.

1. Page 5: Very importantly, the authors Liang and Pardee (Science 1992) did not discover the gene MACC1. The cited paper describes a method, not the discovery of the gene MACC1. The gene MACC1 was discovered and named by the group of Stein et al. and published in Nature Medicine 2009. The very fundamental functions and the prognostic value for patient survival were also first demonstrated by this group. Thus, it is mandatory that this fact is clearly addressed and corrected, so that the creatorship is unmistakably clear.

Response:

Thank you very much for your constructive suggestion. We re-check this issue by reviewing the literature. We agree that The gene MACC1 was discovered and named by the group of Stein et al. and published in Nature Medicine 2009. Correspondingly we revised the manuscript as follows:

In Page 1: Line 1 to. Line 4：

"Metastasis-associated in colon cancer-1 (MACC1) is an oncogene that was first identified in 2009 when Stein U et al. first reported the identification and characterization of MACC1 as an tumor-promoting gene in colon cancer and how it is involved in the HGF-MET pathway and promotes tumor growth and metastasis[1]."

2. Page 6: Concerning SH3 domains: these domains may vary in length. In MACC1, this domain is positioned from 552 – 618 aa, and thus longer than 60 aa.

Response:

Thank you very much for your careful work. We revised the manuscript as follows:

In Page 2: Line 3 to. Line 4：

"SH3 domain is a protein domain with amino acid residues…"

3. Page 13: Why did the authors refer to “five types of cancer”? Which types?

Response:

Thank you very much. In order to address what we mean more clearly, we revised the manuscript as follows:

In Page 12: Line 21:

“MACC1 has been studied in more and more kinds of solid tumors.”

Minor: Pagination is missing. The corrections of some typos is desired, e.g. -in the abstract MACCC1 instead of MACC1, -page 8 processes, -page 16 …significantly ?... -page 18 MACC1 is a mediator…

Response:

Thank you very much for your careful work. Correspondingly we corrected the typos mentioned above when revising the manuscript.