Author's response to reviews

Title: Interrelationship between TP53 gene deletion, protein expression and chromosome 17 aneusomy in gastric adenocarcinoma

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Author's response to reviews: see over
Dear Dr. Whitaker,

We are very grateful to the reviewers of our manuscript.

List of answers to comments of Reviewer 1:

Q1. Referee 1 felt that your study could not clarify the role of the mutations in the early development of gastric cancers. Although you have responded to this point in your covering letter, we would ask that you discuss this limitation in the manuscript text.

Answer: We agree with the Referee that our study did not clarify the role of the TP53 mutations in the early development of gastric cancers. This was not our main objective. We believe that further investigations concerning TP53 mutations should be done in a larger sample, also including early gastric cancer. Thus, we performed some modifications in the final paragraph of the discussion section to reinforce this idea.

“The p53 expression was also associated with a higher frequency of cells with two chr17 and two TP53 signals in intestinal-type GC. We hypothesize that these cells may present TP53 with mutations and this event could be occurring earlier than allelic deletion in intestinal-type gastric carcinogenesis. Further investigations concerning TP53 mutations and expression should be done in larger samples, also including early GC specimens.”

2) With regard to the revised discussion (Referee 1, Q3), the following phrases are unclear and require grammatical improvement:

"could be occur early than allelic deletion in intestinal-type gastric carcinogenesis?"

Answer: Please, change to: “could be occurring earlier than allelic deletion in intestinal-type gastric carcinogenesis”

"On the other hand, loss of TP53 was not coupled with mutations or mutations in the remaining allele can not be detected by immunohistochemistry in diffuse-type GC."

Answer: Please, change to:

“On the other hand, two possibilities might be considered to the absence of immunoreactivity in diffuse-type GC: this absence was not due to mutations in TP53 gene or an eventual mutation in this gene would not interfere in the protein accumulation. In both situations the immunoreactivity cannot be detected.”