13th of January 2014

Dear Editor,

Please find enclosed the edited manuscript.

Title: Proteomic and metabolic prediction of response to therapy in gastric cancer.

Author: Michaela Aichler, Birgit Luber, Florian Lordick, Axel Walch

Manuscript No: 7978

The manuscript has been improved according to the suggestions of reviewers:
1. Missing explanations of abbreviations have been added.
2. Revision has been made according to the suggestions of the reviewer (No00033010). Please find attached our answers to the reviewers´questions. All comments of the reviewer are discussed in detail and are listed point-by-point below.
3. Differentiation between certainties and perspectives of biomarkers has been emphasized.
4. More comments and references on mass spectrometry of paraffined samples are discussed.
5. A part of methods for proteomics was included into the manuscript in the introduction of proteomic analysis for therapy response prediction.
6. Further comments on HER2 which have made the way from basic science to the clinics as well as developments on other targeted therapies and biomarkers which are in the status of basic science have been added.
7. All editorial suggestions have been included.

We thank the reviewer for the helpful comments to improve the manuscript.

Sincerely yours,

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Point-by-point response to the reviewer:

The paper of Aichler et al emphasizes the growing interest of obtaining reliable new markers of gastric cancer for predicting chemotherapeutic and biological treatment response. Authors suggest that new insights may be given by Proteomic Biomarkers. The manuscript is well written and suggests fascinating hypotheses, however some minor objections may be moved:

? Some abbreviations are not fully explained in the text.

Answer: Thank you very much for this hint. We now provide explanations for all abbreviations.

? Apart from epidermal growth factor receptors, other biomarkers appears to be not still well supported by clinical data. This concept needs to be emphasized with a clear differentiation between certainties and perspectives.

Answer: We included more information on HER-targeted therapy and the approval for the use in the clinic as well further targeted therapies without approval (page 6-7). The title of the biomarker section has been changed to emphasize that this section deals more with potential biomarkers (page 8-9). We hope, that now the differentiation between certainties and perspectives becomes more clear.

? The mass spectrometry of paraffined samples appears to be a very interesting approach which should be better explained, since some details are referred to a poor bibliography (two references). A potential tool that could change the future deserves a more detailed debate.

Answer: More comments and references on mass spectrometry of paraffined samples are discussed (page 11) .

? The expansiveness of the methods used for proteomic should be considered and a comment is needed.

Answer: A part of methods for proteomics was included into the manuscript in the introduction of proteomic analysis for therapy response prediction (page 10-11).

? In conclusion, the basic science information and the clinical practice could be better conjugated.

Answer: Further comments on HER2 which have made the way from basic science to the clinics as well as developments on other targeted therapies and biomarkers which are in the status of basic science have been added.