Author's response to reviews

Title: RASSF1A protein expression and correlation with clinicopathological parameters in renal cell carcinoma

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Responses to the comments of A. Sgambato:

Minor revisions:

1. In the revised version of the manuscript the Authors have added the following sentence: “This indicates that higher expression of RASSF1A was positively correlated with the higher pT stage, histological grading, and pTNM group stage in the entire study group irrespective to the labeling index”. What the note: “…..irrespective to the labeling index” means should be clarified.

   This issue has now been improved in the revised version of the manuscript. The following phrase has been removed to avoid misunderstanding: “Irrespective to the labeling index.” Furthermore we have added the phrase “( % labeling index)” in the first sentence of this paragraph to emphasize that cut off value has not been applied for this part of statistical evaluation in order to avoid loss of statistical information.

2. In the revised sentence: “Analysis was carried out for 187 patients with complete follow-up data and pathologically proved clear cell carcinoma of RCC”, I would change the last expression: “clear cell carcinoma of RCC”. This mistake has now been corrected.

3. It is better to indicate in the text that eighteen patients without primary metastasis developed metastases in the course of follow up, otherwise for the readers will not be clear from where the number 35 in Table 2 for patients M1 comes from since in the text is stated that “Seventeen patients demonstrated metastasis at the time of diagnosis.............”. and is not specified how many showed metastasis in the course of follow-up.
In the revised manuscript we have added that 18 patients developed metastases in the course of follow up: “However, eighteen patients without primary metastasis developed metastases in the course of follow up.”

**Discretionary Revisions**

1. **It might be better to show Figure 2 as percent survival rather than as cumulative Hazard over time.**

   We believe that in Figure 2 demonstration of cumulative hazard over time is statistically as representative as percent survival. Thus we preferred to stay with the current version of figure 2.
Responses to the comments of R. Dammann

Major revisions:

1. I suggest that a representative figure for the immunohistochemical analysis of the tissue microarrays should be presented. The paper of Peters et al 2007 does not show a figure with a tumor of high RASSF1A expression (labeling index >25%) compared to a tumor with low RASSF1A expression (<25%). Therefore these data should be shown.

   We now added a new figure (fig 1 A, B) which demonstrates expression of RASSF1A with labeling indices of more and less than 25%. This issue has been noted in the text as well as in the legends to the figures. Consequently numberings of former figures 1 and 2 have been changed.

Minor essential revisions

1. Title of table 2 could be improved: 'Relationship of high RASSF1A labeling index (>25%) and clinicopathological parameters for the entire study group (n=318)'

   The title of the table 2 has been changed as following: “Relationship of high RASSF1A labeling index (>25%) and clinicopathological parameters for the entire study group (n=318)"

2. Figure 1: Add (%) to the x-axis and (cases) to the y-axis.

   In the revised manuscript we added (%) to the X-axis and (cases) to the y-axis