Author’s response to reviews

Title: Dissecting TSC2-mutated renal and hepatic angiomyolipomas in an individual with ARID1B-associated intellectual disability

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Author’s response to reviews:

Dear Editor,

Please find enclosed a revised version of our manuscript entitled “Dissecting TSC2-mutated renal and hepatic angiomyolipomas in an individual with ARID1B-associated intellectual disability”.

Changes in the manuscript text are marked by the “track changes” function of word. We thank the reviewers for their positive evaluation and helpful comments which we addressed as follows:
Reviewer 1:

1. If the patient should be diagnosed as TSC? According to the criteria of International Tuberous Sclerosis Complex Consensus Group in 2012, TSC can be diagnosed with a finding of pathogenic TSC gene mutation, two main characters, one main character and two minor characters.

   - For a definite diagnosis of TSC either a pathogenic mutation, two major clinical findings or one major plus at least two minor findings are required (PMID: 20301399). Our patient has only one major finding (renal angiomyolipoma), and the TSC2 variant could only be detected in tumor tissue but not in any of the unaffected tissues. We therefore would consider “TSC2-associated angiomyolipoma” a more correct diagnosis than “TSC” in her case.

2. TSC mutation can induces mTOR activation, and increases cell growth angiogenesis, and cell migration, which can explain the renal AML and hepatic metastasis AML. Therefore I don’t think that it is necessary to put forward the possibilities in Paragraph 1 in Discussion Section.

   - Listing the possibilities in paragraph 1 of the discussion explains our incentives how to proceed in this special case. We think it would therefore be helpful to leave them in the text to make the following tests and results more comprehensible for the readers. Furthermore, we did not find definite proof for metastasis, still leaving at least an additional possibility (very low-grade mosaicism in kidney and liver).

We hope that our revised manuscript is now suitable for publication in BMC Cancer.

Yours sincerely,

Christiane Zweier