Author's response to reviews

Title: Deletion of the TNFAIP3/A20 gene detected by FICTION analysis in classical Hodgkin lymphoma

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Author's response to reviews: see over
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Editor in chief
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Dear Editor,

I am updating our manuscript because I found I have submitted the revised version of our manuscript entitled 'Deletion of the TNFAIP3/A20 gene detected by FICTION analysis in classical Hodgkin lymphoma ' twice. Please remove # 9309947458016956 from your list and do not regard it as our new manuscript.

At the same time I have updated because I found one of authors is missing in the previous version. Other parts were not changed at all. Thank you taking care of this matter in advance and I hope these revisions satisfied the reviewers.

Sincerely yours,

Yukio Kobayashi
Reply to Dr. Hartmann’s comment:

1. The authors found three cases with a low ratio of TNFAIP3/CEP6 probes in the reactive bystander cells. How do the authors explain this? Could this be due to a technical problem? If a technical problem cannot be excluded, these cases should be noted “not evaluable”.

We omitted the three cases with a low ratio of TNFAIP3/CEP6 probes in the reactive bystander cells. As explained in the original manuscript, the number of available slides was limited and the analyses could not be repeated more than twice. As a result, the numbers of cases in each category were changed and the p-values re-calculated throughout the text. Despite these changes, the result and the major conclusion were not modified, except for the discussion of cHL subtype. The frequency of TNFAIP3 deletion did not increase among NS cases of cHL. This part was omitted from the revised test (see page 10, line 6 from the bottom), and the following text was also revised after exclusion of the three cases: the comment about case #40 on page 10, lines 5-9 and page 12, lines 4-16.

2. The authors state in the introduction "deletion of one allele (of TNFAIP3) has been detected in various B-cell malignancies". The authors should mention, "has been detected in Hodgkin lymphoma and other B-cell malignancies", as deletions of TNFAIP3 have been reported previously in Hodgkin lymphoma and this study basically confirms previous results.

We have changed these sentences according to the reviewer's suggestions. Please see page 4, line 5.

3. The manuscript contains many spelling mistakes and the English is poor. Professional English Editing should be obtained.

We have asked Edanz Editing to edit our paper. We hope this revised version satisfies the reviewers.
Reply to Dr. Kueppers’ comment

1) On p. 4 it is stated that in the present work 9 cases previously analysed and 28 other cases with sequence date were included. However, these number do not add up to the 47 cases studied here. It is also suggested to mark those cases taken from their previous study in Table 1.

We apologize as we made a mistake with our original case numbers. The correct sample characteristics are as follows. 22 of 24 cases have sequence data from a previous study, and 25 further cases were added to this study. We sequenced 6 of these 25 cases. These details are shown in Table 2.

The original number ‘9’ represented cases presented at the ASH meeting 2009, which should have been substituted in this paper by ‘47’, while ‘28’ represented the total number of cases with sequence data in this study including the previous study. Please see page 4, last line of the revised manuscript.

2) At the bottom of p. 8 it is stated that three cases had homozygous deletion. However, that number is six. There were three cases with homozygous deletion and additional sequence information.

As the reviewer points out, this number should have been 6. In this revision of our manuscript, we omitted one of these cases that lacked evaluation of gene status, bringing the number down to 5. The three other cases lacked sequence data and we were unable to sequence them in the present study, probably because of limited DNA. We added a relevant statement to the revised table legends, see Table 2.

3) In the Notes to Table 1, the explanation for the abbreviation "LR" (lymphocyte-rich classical) is missing.

We have added this according to the reviewer’s recommendation. Please see page 21 of the revised manuscript.

During this revision, we have added NS as a co-author.