Reviewer’s report

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

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Reviewer: Ralf Kueppers

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The authors studied 47 cases of classical Hodgkin lymphoma (cHL) for deletions of the TNFAIP3 tumor suppressor gene by FICTION analysis. They detected six cases with homozygous deletion and 15 cases with heterozygous deletion. Compared to their previous analysis for TNFAIP3 mutation by microdissection and PCR analysis they conclude that cases with homozygous deletion have been overlooked, likely because in the microdissection studies are few non-HRS cells are coisolated, giving rise to wildtype sequences and thus a wrong negative result for TNFAIP3 lesions. They conclude that the TNFAIP3 gene is more frequently inactivated by genetic lesions than previously thought and that FICTION analysis is a suitable approach to detect TNFAIP3 deletions in HRS cells.

The definition of homozygous deletion is somewhat debatable, because these cases did not have zero FISH signals for the TNFAIP3 locus, but a signal ratio of TNFAIP3/centromere chromosome 6 of below 0.25. This can be explained by a few cells among the CD30+ cells that are not HRS cells, or by subclonal homozygous deletion events. However, it is also possible that in some cases, there are multiple copies of chromosome 6 and there is still one with the TNFAIP3 gene. In that latter instance, it would be incorrect to call this a homozygous deletion. Nevertheless, the authors discuss this restriction of their analysis in the Discussion.

Minor essential revisions:

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.

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.

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

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.