Reviewer's report

Title: Prognostic significance and therapeutic potential of the activation of anaplastic lymphoma kinase/protein kinase B/mammalian target of rapamycin signaling pathway in anaplastic large cell lymphoma

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Reviewer: Lukas Kenner

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The manuscript Ju Gao et al. „Prognostic significance and therapeutic potential of the activation of anaplastic lymphoma kinase/protein kinase B/mammalian target of rapamycin signaling pathway in anaplastic large cell lymphomas“ is improved, however major points which were pointed out previously and not were not addressed yet.

These are:

Major:

1. Since the AKT1 kinase has two homologs AKT2 and AKT3, it would be interesting to know the respective contributions of these homologs to the AKT/mTOR pathway activation. This should be feasible since there are inhibitors available that bear a certain specificity for the different AKT homologs.

2. In addition the authors should do independent knockdown of AKT1/2/3 using antisense or small hairpin or siRNA techniques in the cell lines mentioned above and study activity of the AKT/mTOR pathway by 4EBP1 and S6K phosphorylation to dissect the differential importance of the homologs.

3. To demonstrate the in vivo significance of their findings, authors should xenograft the above mentioned cell lines into mice and demonstrate the growth pattern and target gene expression levels after mTOR and AKT1/2/3 inhibition.

4. State of the art quantification software (such as Histoquest or else) should be applied to quantify protein expression levels and percentage of tumor/stromal cells affected from the IHC stained tumor samples.

Minor:

1. show p-values in Figs. 3 and 5.

2. The contribution of AP-1 to mTOR signalling should be referenced: Staber et al. 2007.

3. There are still some typos.

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:** Yes, but I do not feel adequately qualified to assess the statistics.