Reviewer’s report

Title: Decreased expression of Yes-associated protein is associated with outcome in the luminal A breast cancer subgroup and with an impaired tamoxifen response

Version: Date: 19 November 2013

Reviewer: Alexander Hergovich

Reviewer’s report:

Lehn et al. study in this report YAP expression levels in the context of different breast cancer subtypes. Furthermore, the authors provide evidence with respect to tamoxifen response and YAP expression levels. Overall, I recommend the following “improvements” of this sound and interesting manuscript:

Major compulsory revisions (major points)

1) In the first paragraph of the introduction, the authors cite three very selective and kind of outdated reviews on YAP. Instead of these references the reviewers should use more recent and outstanding reviews on YAP (e.g. Hong et al. 2012). In the context of references, the authors should also include all relevant references on YAP/TEAD functions in Hippo signalling (e.g. Wu et al. 2008; Zhang et al. 2008; Ota et al. 2008; and maybe also Li et al. 2010; Zhao et al. 2009; Tian et al. 2010; Chen et al. 2010), since currently they cite only one relevant paper (reference 6). Furthermore, the authors also should include the following references in the introduction and/or discussion section: Matallanas et al. (Mol. Cell 2007) and Chen et al. (Nature Med 2012), since these studies showed that YAP levels are decreased in breast cancer samples and that YAP plays a significant role in breast cancer metastasis, respectively.

2) The clinical data look very convincing and are very interesting. However, the data presented in Figure 4 and 5 using the T47D ER+ breast cancer cell line could be expanded with respect to the tamoxifen response phenotype. Personally, it would be interesting to know how MCF7 (another ER+ breast cancer cell line) are affected by YAP siRNA and how YAP overexpression in a standard model cell lines such as MCF10A (either parental ER- or manipulated to express ER) affects the tamoxifen response (maybe YAP overexpression in the T47D cells should also be considered). However, I would also be happy when the authors could explain why they decided to focus on only one cell line in these settings. In my opinion, this point is rather important, since the authors mention the tamoxifen response phenotype also in the title of this manuscript. Moreover, the authors should also speculate more on the observed discrepancy between the ER+ cell line model and primary breast cancer data (see end of 2nd paragraph in the discussion section).

3) In the context of Figure 4, I would also recommend to control for changes in cell cycle progression as a consequence of YAP manipulations by siRNA. It
could be that the general cell cycle is changing in these cells, which might result in a different tamoxifen response, which would indicate that the observed effect is not really directly linked. Therefore, cell cycle profiles and cell cycle markers (such as cyclins D/A/B) should be also examined in these settings.

Minor compulsory revisions (minor points)
A) In the materials and methods section please include the catalogue numbers of the antibodies used in this study, to facilitate the translation of these findings into other ongoing studies.
B) Please improve the labelling of Figure 1, since currently this figure is basically unlabelled.

Discretionary revisions (very minor points)
None

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:
I declare that I have no competing interests.