Reviewer's report

Title: Tumour-associated endothelial-FAK correlated with molecular sub-type and prognostic factors in invasive breast cancer

Version: 1 Date: 14 October 2013

Reviewer: Christina Addison

Reviewer's report:

The authors have shown an interesting correlation with not only tumor cell FAK expression, but also endothelial cell FAK expression levels and tumor type. For the most part the methods and choice of reagents seem appropriate for the analysis that was performed. The main conclusion of the study is that FAK expression is associated with the non-luminal A phenotype of breast cancers, and hence these may be prime candidate tumors for treatment with the novel FAK inhibitors currently in the clinical pipeline.

Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

Despite the fact that this particular FAK antibody clone has been used in other studies for IHC in parafin sections, it would be beneficial for the authors to show IgG negative controls of the antibodies in use to confirm specificity of antibody staining in their hands.

More details are required describing the method of quantitation, for example how many individuals scored the samples and were they scored in a blinded manner?

It is also unclear how the authors "rescaled" the scores for FAK staining, as originally the score for FAK was on a scale of 0-600 and then for comparison, they rescaled from 0-1? How exactly was this done and does one lose sensitivity when doing this type of rescaling?

I am a bit concerned that the sample size of HER2 tumors is extremely biased towards HER2 negative and wonder whether this is influencing the results? It seems odd that a sample size of 12 would give you real clinically significant findings. Can the authors increase the sample size of their HER2 positive group to be less one-sided?

The authors found that there was significant association of FAK expression with increasing age. They should comment on whether there is a biological rationale for this and whether age as a confounding factor was eliminated in their subsequent analyses in all cases.

I find it odd that the authors spend a significant amount of time analyzing the correlations of FAK with the luminal A phenotype as it would seem that it is the lack of FAK that has the association with this phenotype. As such it seems that it is not useful for their end goal, which is to use FAK as a biomarker. They suggest that non-luminal A subtypes would maybe be responsive, but they go on to find
that there is no significant difference between luminal B and non-luminal B subtypes. I would have expected there to be a relationship here in addition to the TN results that they observed. Is this again due to the comparatively small sample size of luminal B compared to others?

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

For some reason, figure 1 is present twice.

For some reasont the authors are really focused on the relationship of low FAK expression with luminal A subtypes, however this has previously been suggested. While it is good to have confirmatory data in other samples, the novelty of this work is potentially the role of the endothelial FAK expression as a putative biomarker. However I felt that the comparison of tumor to endothelial FAK expression, and whether they are equivalent or one is better than the other is a bit lost in the article as much of the focus is on the luminal A results.

Discretionary Revisions (which are recommendations for improvement but which the author can choose to ignore)

Based on the results presented, I do not think that endothelial cell FAK is any better of a biomarker than tumor cell FAK in the context of which breast cancer subtypes will be responsive to FAK inhibitors, and as such, this article is more of a confirmatory paper of previously published data.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**

I have no competing interests to declare.