Reviewer's report

Title: Altered PPP2R2A and Cyclin D1 expression defines a subgroup of aggressive luminal-like breast cancer

Version: 4 Date: 15 January 2015

Reviewer: Stuart Schnitt

Reviewer's report:

This is an interesting paper but has limitations, some of which are discussed by the authors in the final paragraph of the Discussion.

Compulsory revisions:

1. One of the limitations relates to the possible interaction between the PPP2R2A-/low//Cyclin D1 high phenotype and treatment variables, which the authors acknowledge that they did not study. Understanding this interaction and analyzing this in a multivariable model is really needed to determine if this phenotype is a prognostic factor, predictive factor or both. Further, while the authors provide some information about treatment in the Materials and Methods section (p.5), they do not indicate what local therapy the patients received (how many had mastectomy with or without RT, how many had breast conserving surgery with RT), and how many received hormonal therapy with or without chemotherapy.

2. In the second paragraph of the Results, the authors relate the presence of CNA for PPP2R2A to outcome in the TCGA database. Without information about treatment variables and without correction for other adverse prognostic factors with which this CNA seems to be associated these outcome data are not very meaningful. The authors should either provide justification for including these outcome data or remove it.

3. Based on examination of the Kaplan-Meier curves in Figure 5 the Discovery cohort and the Validation cohort seem to have very different outcomes. For example 10 yr DFS seems to be about 90% in the Discovery cohort but less than 70% in the validation cohort. How do the authors explain this?

Level of interest: An article of limited interest

Quality of written English: Acceptable

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

Declaration of competing interests:

I am serve an advisory committee for the first author