Reviewer's report

Title: Merging transcriptomics and metabolomics - advances in breast cancer profiling

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Reviewer: Gema Moreno-Bueno

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The manuscript of Borgan et al, describes the use of transcriptomic and metabolic profiles in breast cancer in order to redefine the subclassification of these tumours and also identify new relations between metabolic and transcriptional level.

Breast cancer has been considered as heterogeneous disease, in fact some years ago it was defined a new molecular classification that included five different subtypes of these tumours (Luminal A, Luminal B, Basal-like, ERBB2 enriched and normal-like). A lot of studies have been focalizing in the identification of new molecular markers or specific pathways that define these carcinoma subtypes. In the present manuscript, the authors combine transcriptomic and metabolic profiling of the samples to identify a comprehensive picture at a specific moment, their studies detected several differences and similarities between group of samples showing that exist a biological dynamics in these carcinomas.

The manuscript is very interesting and has clarified some doubts about the molecular classification of breast cancer and should be considered for publication in this journal. However the following topics need to be revised or clarified:

1.- The authors analysed 46 breast samples, to identify the specific interactions between metabolic and transcriptomic levels, using different breast carcinoma molecular subtypes however in the Table 1 it has been observed that they analysed oestrogen/progesterone receptor positive samples mainly, in this sense their study should be more equalized in order to identify pathways in all of the tumours subtypes. The authors should be adding some tumours without oestrogen/progesterone receptor expression.

2.- The author comment that mainly have detected a luminal A tumors, and this result are correlated with the selection analysed samples. Only detected one sample ERBB2 or basal-like enriched and this results could be derived the pathological characteristic from selected samples. The major question is, what does their analysis provide in comparison with the pathological characteristic of the tumours?, in this sense, could their be study used at other tumors?.

3.- According their results, the author can be subdivided the luminal A tumours in three subtypes (A1-A3) however these results depend the statistical analysis made. In Limma analysis they do not detected different significant genes with
FDR<0.01, however when the author use the GSA analysis detected different enriched GO-Terms. In this sense, whether the results depend on the statistical analysis used, what is the biological relevance of these results?

**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, and I have assessed the statistics in my report.