Reviewer's report

Title: Glycanogenomic analysis of heparan sulfate proteoglycans expression in breast cancer: Identification of specific changes in tumours

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Reviewer: James Whiteford

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In the manuscript by Fernández-Vega et al. the authors address the highly complex problem of establishing whether there are differences in the expression of both HSPGs and HS biosynthetic and modifying enzymes between metastatic and non-metastatic infiltrating ductal adenocarcinomas. The authors use qPCR address this important issue. The methods used in this paper are generally sound and despite a number of factual and grammatical errors in the manuscript this reviewer would recommend publication subject to several changes. These are described below.

Major revisions.
1) The primer sequences described in the methods would be better placed in a supplement.
2) The overall findings of the study suggest there are very few differences between expression of the genes of interested between metastatic and non-metastatic tissue. Are there any marker genes that could be used to validate whether a tissue sample is genuinely metastatic or not? If the authors could demonstrate up or down regulation of such genes this would give confidence that the tissues were in fact different. It is appreciated that syndecan-1 could be used in this way, but for example could a marker of Epithelial to Mesenchymal transition be used?
3) Syndecan antibodies are not regarded as very effective. For this reason an isotype control should be included in the staining in figure 2.
4) The manuscript contains many scientific inaccuracies which should be addressed. For examples the syndecans are not isoforms of each other but separate genes. These in addition to the grammar should be addressed.

Minor Revisions.
1) Although it is highly comprehensive the discussion should be shortened.
2) For the general readership the authors could also include a diagram explaining HS and CS biosynthesis since this is not something which is easily explained.
3) HS sulphation pattern specific antibodies have been generated and these may offer more insight into the differences between metastatic and no-metastatic tissues.
Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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