Reviewer’s report

Title: Glutamate metabotropic receptor 4 (GRM4) inhibits cell proliferation, migration and invasion in breast cancer and is regulated by miR-328-3P and miR-370-3P

Version: 1 Date: 11 Feb 2019

Reviewer: Francesca Peruzzi

Reviewer's report:

The authors performed in silico analysis and showed increased expression of GRM4 in luminal breast cancer. They further demonstrated that GRM4 expression inhibits proliferation, migration and invasion of MCF7 breast cancer cell line. In addition they found that miR-328-3p and miR-370-3p target GRM4 3'UTR and that overexpression of either miRNA into MB-231 cells overexpressing GRM4 result in increased migration and invasion. While this knowledge could be relevant the study could be improved by providing data supporting the biological relevance of miRNA/GRM4 expression, as detailed below.

Specific comments:

1) Please add description to Fig 1D and add Fig.1E to the description of the survival curve in the results section.

2) The authors convincingly show that GRM4 is a target for the two miRNAs. However, it is not clear whether those miRNAs could play a biological role in breast cancer. The data could be strengthened by showing the expression levels of miR-328-3p and miR-370-3p in MCF7, MDA-MB-231 and in clinical samples, and by showing the effect of miRNA mimics and inhibitors on GRM4 expression in MCF7 and MB-231 cell lines, respectively.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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I am able to assess the statistics

Quality of written English
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Acceptable

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