Reviewer’s report

Title: Transcriptomic and ChIP-sequence interrogation of EGFR signaling in HER2+ breast cancer cells reveals a dynamic chromatin landscape and S100 genes as targets

Version: 0 Date: 06 Jun 2018

Reviewer: Ahmad Khalil

Reviewer's report:

This manuscript describes changes in gene expression in HER2-positive breast cancer cells (SKBR3) upon activation of EGFR. The authors use both RNA-seq and ChIP-seq to identify genes that are affected by EGF binding to EGFR and activation of downstream signaling pathways leading to changes in gene expression and chromatin modifications in a time-dependent manner. I would recommend the publication of this manuscript if the authors can address the following:

1. The authors need to clearly state how many replicates of RNA-seq and ChIP-seq were performed at each time point and the appropriate statistical analysis that were done to identify differential gene expression and changes in histone modifications.

2. The section describing ChIP-seq data is very difficult to read and there are too many numbers. You can add a table to simplify.

3. The authors should cite a few more papers that discuss trastuzumab-resistance that are relevant to their findings.

4. In general, the manuscript would benefit from editing for clarity.

I think this an important manuscript to the field if these concerns can be corrected.
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?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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