Reviewer’s report

Title: Leptin-induced ER–Positive Breast Cancer Cell Viability and Migration is mediated by Suppressing CCN5-Signaling via Activating JAK/AKT/STAT-pathway

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Reviewer: Young Suk Jo

Reviewer's report:

The authors have observed the effect of leptin on epithelial-mesenchymal transition (EMT) and suggested that the transcriptional suppression of CCN5 by leptin might be a underpinning mechanism in ER positive breast cancer. But, the data interpretation need to be clearer because the experimental findings presented in this paper did not show the direct mechanistic relationship between CCN5 and leptin. In fact, the data just indicated competitive antagonistic effect of GCN5 on leptin action and vice versa.

Major Revisions

1. Figure 1: The authors said that the CCN5 expression can be repressed in MCF-7 and ZR-75-1 cells by leptin treatment. To support this idea, the authors presented data from Northern blot, qPCR, Western blot and CAT assay. However, the author did not show any evidence showing if the leptin treatment was properly working in both cell lines or not. The authors said that leptin can stimulate JAK/STAT3, ERK1/2 and PI3K pathways. The authors at least presented which kind of signal pathway was able to be activated in both cell lines by leptin treatment. After they find major signal pathway activated by leptin, the authors may want to perform inhibitor studies to verify leptin-induced CCN5 transcriptional repression.

2. Figure 2 and 3: Again, the authors need to present the signal pathways involved in leptin-induced cell proliferation, invasion and migration combined corresponding inhibitor studies. Unfortunately, the data in these figures did not show leptin-induced CCN5 transcriptional repression. They have shown the repression of leptin effect on cell biology by CCN5. This issue is quite important because the title of this paper is "Leptin-induced ER--Positive Breast Cancer Cell Growth and Migration is mediated by Suppressing CCN5-Signaling". The authors need to show the results from new experiments showing the effect of leptin treatment on CCN5-null systems.
Minor Revisions

1. Figure 2: The data on this figure did not show the dose dependent effect of leptin, but presented time-dependent effect. Please check the description for this figure (Page 13, Line 3).

2. Figure 4B: The authors may want to present p-values.

3. Figure 5: The summary figure is not based on the data presented in this paper. It should be revised properly after revision experiments.

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

No

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

No

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

No

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.

Not relevant to this manuscript

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

Acceptable
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