

## Format for ANSWERING REVIEWERS

March 17<sup>th</sup>, 2015



World Journal of Biological Chemistry

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 16688-edited.docx).

**Title:** Adipocyte Activation of Cancer Stem Cell Signaling in Breast Cancer

**Author:** Benjamin Wolfson, Gabriel Eades, Qun Zhou

**Name of Journal:** World Journal of Biological Chemistry

**ESPS Manuscript NO:** 16688

The manuscript has been improved according to the suggestions of the Editor:

1. Format has been updated
2. Figure has been redone as PowerPoint file, uploaded separately in file entitled "figure 1.ppt"
3. For references for which DOI or PMID numbers are not available, the first page of the manuscript has been uploaded separately per your request.

Revision has been made according to the suggestions of the reviewers

*Reviewed by 02799783*

The authors discuss the involvement of adipocytes in the microenvironment and breast cancer cells. They defend the idea that adipocyte-secreted leptin and IL-6 in inducing breast cancer cell epithelial-mesenchymal transition and activating new pathways. They raise new therapeutic possibilities in tumor microenvironment and the possibility of using non-coding RNAs through interaction with tumor cells. I recommend the manuscript for publication in the World Journal of Biological Chemistry.

**We appreciate the reviewer's suggestion for publication.**

*Reviewed by 02800292*

Well-written review article summarizing the relationship between adipocytes in the microenvironment and breast cancer cells, emphasizing on the role of adipocyte-secreted leptin and IL-6 in inducing breast cancer cell EMT and activating stemness pathways. The authors should be congratulated for their effort and the review article deserves to be published. Minor comments:

**We appreciate the reviewer's comments, and have addressed them in the refined paper.**

1) Information regarding experiments performed on the differential expression of miRNAs in adipose tissue after long-term high-fat diet-induced obesity in mice should be included in the text (PLoS One. 2012;7(4):e34872).

**We have added discussion of differential miRNA expression in obese adipocytes and the supplied reference to our manuscript.**

2) In the last paragraph, perhaps the authors could emphasize on the role of the miR-200 family on EMT.

**We have added discussion of the role of miR-200 family in EMT to the paragraph specified.**

*Reviewed by 02613582*

In this review, Wolfson et al summarize major signaling pathways that regulate cancer stem cells in breast cancer, describe the effects of IL-6 and leptin secreted by adipocyte on breast cancer stem cell signaling, and introduce a potential treatment paradigm of inhibiting the adipocyte-breast cancer cell signaling via targeting the IL-6 or leptin pathways. This in itself is a significant contribution.

**We appreciate the reviewer's comments, and have addressed them in the refined paper.**

1. The authors appear to be trying to focus on signaling pathways regulating cancer stem cells in breast cancer and effects of IL-6 and leptin secreted by adipocyte on breast cancer stem cell signaling. However, there is too little review on the main topic. It will better the author adjust the articles proportion and make it more logical.

**As the format of this manuscript is a mini-review, we chose to focus on the role of the IL-6 and leptin pathways in adipocyte-breast cancer stem cell signaling, as opposed to doing a more comprehensive review of adipocyte-breast cancer signaling pathways. In part due to the newness of this research field, and in part due to the need to provide proper context, the ratio of background may have been disproportionate. We agree with the reviewer and in light of this comment have amended our discussion of the main topic and provided additional thoughts on where the field might be going next.**

2. Needs some language corrections before being published.

**We have edited the manuscript for language use.**

3. The obvious mistakes that I noted have been highlighted in the accompanying file.

**We did not find this file and asked the Editor office for the accompanying file. However, the specified file was not available. We have edited for language use.**

Thank you again for publishing our manuscript in the World Journal of Biological Chemistry

Sincerely,

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