

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 46740

**Title:** BREAST CANCER STEM CELLS: THE ROLE OF SEX STEROID RECEPTORS

Dear reviewer,

many thanks for your suggestions; with them, I have ameliorated my manuscript.

*Authors should consider including one or more figures illustrating the pathways affected by steroid hormone receptors leading to the generation of breast cancer stem cells.*

I have added a figure representing the main pathways activated by estrogen receptor isoforms in breast cancer stem cells. In this figure, I have considered only the pathways explored in breast cancer stem cells and not the hypothetical ones.

*The authors might consider reorganizing the material in a way that indicates the nuclear hormone receptors associated miRNAs that regulate the process of breast cancer stem cell development in a separate section.*

Now the manuscript has a new section entitled: Steroid receptor-regulated miRNAs in BCSCs. Thanks you for this suggestion.

*A paragraph indicating future directions should be included.*

The last paragraph is now entitled: Concluding remarks and future directions and includes some considerations about the use of sex steroid receptors in breast cancer cells as molecular target for future therapies.

*Minor comments Estrogen receptor instead of estradiol receptor throughout the manuscript*  
Done.

*"The two ER subtypes are encoded by genes on different chromosomes and activate estrogen response elements (ERE) in gene reporter assay (32)." Do the two different types of ER regulate the expression of the same genes?*

I have changed this sentence in: The two ER subtypes are encoded by genes on different chromosomes and differentially activate common estrogen response elements (ERE) in gene reporter assay (32, 33) and add a new ref: Zhao C, Dahlman-Wright K, Gustafsson JÅ. Estrogen signaling via estrogen receptor {beta}. J Biol Chem. 2010 Dec 17;285(51):39575-9. doi: 10.1074/jbc.R110.180109. Epub 2010 Oct 18. Review. PubMed PMID: 20956532.

*Some more details on the pathways affected by the ERα and how proliferation and aggressiveness are regulated by this receptor would be beneficial for the quality of the review.*

Done. I've enriched this paragraph. Many thanks for this suggestion.

*"non-CSTs (44)" ? "a granzime B" ? "...two important transcription factors implied in the control of mammary cell fate (60)." Implicated instead of implied? "BCSTs" ? Although the interest in the study of BCSCs is currently "blown up"?, it is not yet well known how these cells work within the cancer and what are the engaged pathways. "contributing to cell de-differentiation cells"*

I have corrected all the mistakes. Thank you.

I hope I have done everything better. Thank you again

Sincerely

Pia Giovannelli