

We thank the editor and reviewer for your useful suggestions that helped our manuscript improve.

RESPONSE TO PEER-REVIEW REPORT

- **Reviewer#1. Minor concern:** - page 5, line 7: The authors claim that “changes in the cellular phenotype lead tumor cells to invade the surrounding matrix,...”. Invasion is due to changes in the cellular biological properties (which includes cellular phenotype), as cells are subjected to an epithelial-to-mesenchymal transition (EMT). The text should be modified accordingly.

Response: We changed “cellular phenotype lead...” by “cellular biological properties lead...”.

SCIENCE EDITOR COMMENTS AND SUGGESTIONS

- **Comment 1:** (5) Self-cited references: There are 13 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations.

Response: We removed 4 of our self-references and reordered the rest of the references. We removed the references numbered:

83 **Español** AJ, Sales ME. Different muscarinic receptors are involved in the proliferation of murine mammary adenocarcinoma cell lines. *Int J Mol Med* 2004; **13**: 311-317 [PMID: 14719140 DOI: 10.3892/ijmm.13.2.311].

84 **Español** AJ, de la Torre E, Fiszman GL, Sales ME. Role of non-neuronal cholinergic system in breast cancer progression. *Life Sci* 2007; **80**: 2281-2285 [PMID: 17276463 DOI: 10.1016/j.lfs.2006.12.017].

151 **Sales** ME. Muscarinic receptors as targets for metronomic therapy in breast cancer. *Curr Pharm Des* 2016; **22**: 2170-2177 [PMID: 26924207 DOI: 10.2174/1381612822666160229115317].

152 **Negroni** MP, Fiszman GL, Azar ME, Cresta Morgado C, Español AJ, Pelegrina LT, de la Torre E, Sales ME. Immunoglobulin G from breast cancer patients in stage I stimulates muscarinic acetylcholine receptors in MCF7 cells and induces proliferation. Participation of nitric oxide synthase-derived nitric oxide. *J Clin Immunol* 2010; **30**: 474-484 [PMID: 20157846 DOI: 10.1007/s10875-010-9370-0].

- **Comment 2:** 5 Issues raised: (1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

Response: We provide a founding agency file name “64445-Approved grant application form (s)”

of funding agency copy of any approval document (s)".

- **Comment 3:** The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;

Response: We provide file with original figures with the name: "64445-images 1-2-3 file".

- **Comment 4:** (3) If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights

Response: all figures were made by us.

ADDITIONAL INFORMATION FROM THE AUTHORS

- We reordered all references since we removed some of these.
- We modified figure 1 for a better understanding
- We attach different requested files.