Author's response to reviews

Title: Rac3 induces a molecular pathway triggering breast cancer cell aggressiveness: Differences in MDA-MB-231 and MCF-7 breast cancer cell lines.

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To the editor of BMC Cancer

Dear Editor,

We would like to submit the manuscript, “Rac3 induces a molecular pathway triggering breast cancer cell aggressiveness: Differences in MDA-MB-231 and MCF-7 breast cancer cell lines” for publication in BMC Cancer.

In this paper, we analyze the role of Rac3 GTPase in the different criteria of breast cancer cell aggressiveness and examine the biological mechanisms by which expression of Rac3 may exert an effect in cells in which RhoA is more or less overexpressed and constitutively activated. Most of the literature addressing the role of Rac in cancer aggressivity concerns Rac1, and studies on the role of Rac3 in cancer progression are far less abundant. In this work, we examined the effects of Rac3 down-regulation by siRNA treatment in invasive MDA-MB-231 and non-invasive MCF-7 cell lines which both express Rac3. The major point of this work is the observation that despite the low expression of Rac3 in breast cancer cells these GTPase is involved in the cancer cell’s aggressiveness even when RhoA is activated. In
MDA-MB-231 cells, Rac3 inhibition caused a reduction of invasion, cell adhesion and an increased in TNF-induced apoptosis. However, Rac3 does not influence any parameters of aggressiveness in MCF-7 cells. To explain this discrepancy, we propose a signaling pathway. In MDA-MB-231 cells, the aggressiveness dependent of Rac3 is due to the Rac3/ERK-2/NF-kappaB signaling pathway. This pathway is not functional in MCF-7 cells because NF-kappaB is low expressed in these cells.

Thank you in advance for considering our manuscript for publication in *BMC Cancer* and we look forward to hearing from you.

Sincerely yours,

Hong Li