

PEER-REVIEW REPORT

Name of journal: *World Journal of Clinical Oncology*

Manuscript NO: 74097

Title: Nicotinic receptors modulate antitumor therapy response in triple negative breast cancer cells

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05194763

Position: Peer Reviewer

Academic degree: MSc

Professional title: Research Scientist

Reviewer's Country/Territory: Italy

Author's Country/Territory: Argentina

Manuscript submission date: 2021-12-27

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-12-27 12:33

Reviewer performed review: 2022-01-09 16:07

Review time: 13 Days and 3 Hours

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|--------------------|---|
| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| Conclusion | <input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |

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| Peer-reviewer statements | Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No |
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SPECIFIC COMMENTS TO AUTHORS

The manuscript by Español et al aims to investigate the effects of nicotine on paclitaxel treatment using MDA-MB231 as an in vitro model of triple negative breast cancer. Since this breast cancer subtype is the one for which no effective targeted therapies has been yet identified, it represents a matter of concern in the clinical practice. Hence, studies concerning the effect of exposition to factors on therapy are precious. They found that the action of nicotine is responsible of the reversion of the cytotoxic effect of paclitaxel in MDA-MB231 cell lines and reduction of cell apoptosis. The nicotinic acetylcholine receptors (nAChR) are considered the reponsible for the decrease of the effect of paclitaxel and the authors legitimately suggest to consider them as targets in smoking patients. This is a very good paper, well written and with a good level of English. Moreover, I think that the methods are proper for their aims. The results are adequately described, finally I think that this article should be considered for publication in World Journal of Clinical Oncology. I only have one comment: -Please check this sentence: "After treatment, the medium was removed and 100 μ L of MTT solution (500 mg/L medium free of phenol red and FBS)". It sounds incomplete.

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Reviewer's code: 06135401

Position: Peer Reviewer

Academic degree: MD, MSc

Professional title: Assistant Professor, Senior Postdoctoral Fellow, Senior Researcher

Reviewer's Country/Territory: Egypt

Author's Country/Territory: Argentina

Manuscript submission date: 2021-12-27

Reviewer chosen by: Ze-Mao Gong

Reviewer accepted review: 2022-01-15 16:56

Reviewer performed review: 2022-01-23 10:48

Review time: 7 Days and 17 Hours

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| Scientific quality | <input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish |
| Language quality | <input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection |
| Conclusion | <input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection |
| Re-review | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |

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|-------------------------------------|---|
| Peer-reviewer statements | Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No |
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SPECIFIC COMMENTS TO AUTHORS

I really appreciated the effort made by the authors in addressing such an important and novel topic in Nicotinic receptors modulate antitumor therapy response in triple negative breast cancer cells . I've found the work is well written and informative. However the following comments is required: In introduction section, activation of nAChRs induce an increase in intracellular calcium levels[14], which may in turn activate different signaling pathways. What is the applied clinical pathophysiology in tumorigenesis which was proved in literature in induction of cancer in different organs by disruption of this pathway? An illustration of cell culture, viability assay and uses of western blot by a figure or a diagram is recommended

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Reviewer's code: 05325611

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Argentina

Manuscript submission date: 2021-12-27

Reviewer chosen by: Ze-Mao Gong

Reviewer accepted review: 2022-01-20 11:32

Reviewer performed review: 2022-02-01 15:11

Review time: 12 Days and 3 Hours

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|---------------------------|---|
| Scientific quality | <input checked="" type="radio"/> Grade A: Excellent <input type="radio"/> Grade B: Very good <input type="radio"/> Grade C: Good <input type="radio"/> Grade D: Fair <input type="radio"/> Grade E: Do not publish |
| Language quality | <input type="radio"/> Grade A: Priority publishing <input checked="" type="radio"/> Grade B: Minor language polishing <input type="radio"/> Grade C: A great deal of language polishing <input type="radio"/> Grade D: Rejection |
| Conclusion | <input type="radio"/> Accept (High priority) <input checked="" type="radio"/> Accept (General priority) <input type="radio"/> Minor revision <input type="radio"/> Major revision <input type="radio"/> Rejection |
| Re-review | <input checked="" type="radio"/> Yes <input type="radio"/> No |



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| Peer-reviewer statements | Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] No |
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SPECIFIC COMMENTS TO AUTHORS

Overall, this is an interesting work to investigate the effect of nicotine on paclitaxel treatment TNBC cell line and the potential regulating signaling pathways. The therapeutic effect of paclitaxel may be affected by nicotine, which is a clinical problem that needs to be elucidated. More importantly, the finding may shed light on the critical role of nicotine during treatment of other tumor types in smoking patients. This manuscript is suggested to be accepted after minor revision.