Author's response to reviews

Title: Estrogen-Induced DNA Synthesis in Vascular Endothelial Cells is Mediated by ROS Signaling

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Thank you very much for the review of our manuscript entitled "Estrogen-Induced DNA Synthesis in Vascular Endothelial Cells is Mediated by ROS Signaling" (MS# 2079002372829839). Please find enclosed our revised manuscript. We have incorporated most of the suggestions of the reviewers in the text.

Reviewer #1 Discretionary Revisions (which author can choose to ignore)
The involvement of ROS in E2-induced ROS proliferation is not very well proved. If it is receptor mediated, why is the increase sustained 90 min after stimulation? Are the levels similar to those at 5 min? The time course should be presented.

We have already published these data in other cell lines please see reference [1].

Where is the author's hypothesis that it could be integrin-mediated based? Is there anything on the literature or just speculation?

We have previously published the integrin mediated E2-induced ROS please see references [1-3]. The integrin mediated ROS mechanism is in the literature and we have added their references 30-32 to the final manuscript.

Any physiological significance of the pro-oxidant effect at low concentrations and antioxidant on high?

We have previously published the significance of prooxidant effects such as control of cell cycle progression, cell survival/growth please see references [1,2,4].

Since there are no good pharmalogical tools, the authors could use genetics to suppress e.g. estrogen receptor expression.

We have already established in other cell lines that E2-induced ROS is not dependent on the ER please see reference [1]. And this is beyond the scope of this paper.

Reviewer #2 Discretionary Revisions (which author can choose to ignore)
The authors mention that they have carried out experiments using adenoviral MnSOD and catalase. It would be interesting to include these in this study; as it is quite within the scope of this work and that would significantly improve this paper.

Our preliminary data will take several months to complete and I do not think it is necessary for this paper.

Reference List