Reviewer's report

Title: Hyperoxia retards growth and induces apoptosis and loss of glands and blood vessels in DMBA-induced rat mammary tumors

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Reviewer: sallie schneider

Reviewer's report:

General
This manuscript is an extension of a previously published experiment showing that hyperbaric hyperoxic conditions may be beneficial for the treatment of tumors and in fact may work additively or synergistically with 5-FU to cause regression of tumors. In this case, the authors are concentrating on whether hyperoxic conditions or hyperoxic with low hyperbaric conditions can also be used to inhibit the growth of tumors. Their first figure suggests that hyperoxic normobaric or hyperbaric hyperoxic conditions for 90 mintes every couple of days can in fact retard the growth of the DMBA induced tumors. The can also show that there is more apoptosis in these tumors under hyperoxic conditions and a lower microvascular density although diameter appears to increase. These results reflect their previous results and it will be interesting to see the kind of effects they get with hyperoxic conditions and other types of chemotherapeutic reagents. The paper also goes on to make two interesting observations 1) that the tumor tissue develops large empty spaces after treatment and 2) that there is a strong decrease in glandular secretory proteins. The microarray data was verified by RT-PCR analysis.

The experimental system appears to be sound and well controlled. I would say their first paper was more exciting because they could show actual regression of tumors, but these experiments fine tune their parameters. The authors attempted to add a novel part to this story by presenting the observation of the "holes" in the tissue and the decrease in glandular components. At this point, the paper becomes a bit weaker. While they can confirm the gene expression changes, it is not clear to me whether this is an important change or whether it might explain the "holes". They seem to want to suggest that the holes are due to a decrease in normal gland tissue but this is not proven or even examined in detail. Further IHC studies to look at normal versus tumor biomarker might help, or a time course, or possibly the examination of what hyperoxic treatment does to syngeneic tumor grafts which does not contain normal tissue embedded in the tumor. It makes me wonder what happened to the normal glands after treatments as well.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
My concern is that this paper represents only an incremental increase in our understanding from their last paper, albeit an apparently sound scientific observation. I think it would help us to see how the normal gland responded to the hyperoxia and possibly IHC for the glandular components to see where they are expressed in the tumor tissue.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No
Declaration of competing interests:

I declare that I have no competing interests.