Reviewer's report

Title: Analysis of the Effects of Exposure to Acute Hypoxia on Oxidative Lesions and Tumour Progression in a Transgenic Mouse Breast Cancer Model

Version: 1 Date: 10 September 2007

Reviewer: Paul Henderson

Reviewer's report:

General
This is a substantial examination of the effects of hypoxia on tumor progression in a polyoma virus middle T mouse model of breast cancer. The authors compared the effects of acute hypoxia against an air-only control using a well-controlled study with endpoints that included tumor size and metastasis, 8-oxodG and lipid peroxidation measurement, BER activity, vasculature, hypoxia induced factors and tumor associated macrophages. The most interesting finding is that hypoxia increases 8-oxodG, lipid peroxidation and tumor associated macrophages (TAMs), but with little effect upon tumor progression. The results, in part, contradict those reported in a separate paper (also in review) by the same group with a different mouse model (8-oxodG decreased with hypoxia, and hypoxia caused a slowed tumor progression, but an increase in lung mets). This contradiction highlights the importance of performing this work in multiple models. The authors conclude that hypoxia-induced increases in 8-oxodG and TAMs. The work should be published without further experiments, but lacks a bit of discussion as elaborated below.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
A critical discussion of the 8-oxodG and lipid peroxidation measurements should be included. The changes in these products, while statistically significant, may not be great enough to have a biological impact. Since they are ubiquitous in cells, 8-OxodG and lipid peroxidation may play a role in tumor progression, even though it is not obvious from this study. The contribution to tumor progression by other DNA adducts is not assessed by this study. Those experiments are outside the scope of this work, but discussion of the possibility is warranted. The strong phenotype of the mouse model toward early tumorigenesis, though the tumors are closer to humans histologically than many other models, may be too potent to allow characterization of the impact of DNA damage on tumorigenesis as it occurs in WT animals and humans.

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

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Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests