Reviewer’s report

Title: Ascorbic Acid and Ascobate-2-Phosphate decrease HIF activity and malignant properties of human melanoma cells

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Reviewer: Constance E Brinckerhoff

Reviewer’s report:

In this paper, the authors describe the ability of ascorbic acid and ascorbate-2 phosphate (an inhibitor) to decrease HIF activity in human melanoma cells. For the most part, the paper is clearly written and the rationale for the experiments clearly stated.

Major Compulsory Revisions:

1. The major concern, which must be addressed, is the statement by the authors that they have used physiological concentrations of ascorbic acid.
2. There is no reference given as to what these physiological concentrations are.
3. In Figure 1, they see a substantial effect with 25 uM, but also use concentrations up to 100uM (10^-4M). This seems very high and one wonders what levels are actually achievable in vivo.
4. Other experiments also use very high concentrations of both ascorbic acid and the inhibitor.
5. The size of the HIF promoter construct should be stated.
6. The sequence of the construct and the putative response elements should be illustrated.

The author must respond to these before a decision on publication can be reached. For example, additional necessary experiments or controls, statistical mistakes, errors in interpretation.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests'