Reviewer's report

Title: Molecular targets for the protodynamic action of cis-urocanic acid in human bladder carcinoma cells

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Reviewer: Rebecca Riggins

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This is an interesting and very well-written paper that begins to elucidate the mechanism by which cis-urocanic acid can inhibit the growth of human bladder cancer cells. A small number of minor (but essential) revisions are listed below.

1. Discussion, page 15: In the second paragraph, the authors discuss the novelty of using a phosphatase-inhibiting agent to kill cancer cells, and make the connection between increased phosphatase 2A activity and mutant H-Ras. While they cite evidence that transitional cell carcinoma has H-Ras mutations (manuscript reference 16), H-Ras mutation in other types of bladder cancer and in bladder cancer cell lines (including 5637) is quite rare (see Knowles and Williamson, Cancer Research 53:133-39, 1993). Therefore, it is unclear how widely applicable this mechanism might be.

2. Conclusions, page 16: In the first sentence of this section, the authors state “…our study describes the cytotoxic effects of cis-UCA in bladder carcinoma cells…” While evidence in support of cytotoxicity (i.e. cell death) is clearly demonstrated, it is also clear that cis-UCA has a cytostatic (i.e. cell cycle inhibitory) effect as well (shown in Figure 3). This should be clarified or stated here.

3. While statistical analysis is presented for some experiments, its application seems rather selective. Figures 3, 4A, and 4C should also show statistical analyses, p values, etc. In addition, are the data from Figure 1 generated from multiple experiments? If so, statistics should be shown here as well.

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.