Reviewer’s report

Title: The Nrf2-mediated oxidative stress response pathway is associated with tumor cell resistance to arsenic trioxide across the NCI60 panel

Version: 2 Date: 26 April 2010

Reviewer: Chris Corton

Reviewer’s report:

Liu et al.

This manuscript describes the identification of genes that are associated with responses to arsenic in human cancer cell lines. The authors use data available through the web to identify genes that exhibit positive or negative correlations with cytotoxicity caused by treatment with arsenic. The major finding was that a number of these genes appear to be regulated by Nrf2. Support for this hypothesis comes from previous work which indicates that Nrf2 can act as a double-edged sword in protecting the tumor cells from killing by chemotherapeutic agents.

The authors have presented data which supports the hypothesis that Nrf2 is activated in a number of cell lines. However, other pathways which regulate these same genes could be envisioned including activation of CAR or PXR. To help support their hypothesis, the authors should examine the nuclear accumulation of Nrf2 in a set of cell lines that exhibit differences in the expression of target genes. The authors should also knockdown Nrf2 expression in a resistant cell line and determine if arsenic sensitivity is altered.

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'