Reviewer's report

**Title:** Characterization of the Apoptotic Response of Human Leukemia Cells to Organosulfur Compounds

**Version:** 1  **Date:** 12 April 2010

**Reviewer:** John Pinto

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The submitted manuscript by Wong, Boutros, Wasylishen et al entitled: Characterization of the apoptotic response of human leukemia cells to organosulfur compounds, describes a paradigm for drug discovery and design by combining the efforts of laboratories with expertise in synthetic organic chemistry and in molecular biology. The manuscript examines the potential chemotherapeutic mechanisms of action of a variety of organosulfur compounds the efficacy of a few have been previously studied. This manuscript extends the molecular features of the organosulfur analogues newly synthesized and characterized for efficacy in a variety of tumor and non-cancerous cell lines. In view of the comparative aspects describing the antiproliferative effects in leukemic (other cancerous cells) as well as in “normal fibroblast” cell lines, the title should be modified to reflect this comparative analysis of cells using these organosulfur compounds.

The manuscript is adequately written and presents a number of important considerations and insights when conducting comparative analysis of organosulfur analogues. The methods of MMT assay, cell cycle analysis, and microchip array are well established. However, several major and minor considerations need to be addressed. For simplicity, the reviewer will present them by page number

Pg 6

MTT assays “were”

The volume of acetone used in control cultures should be noted in the MTT assay and microarray assay.

The use of a plural verb should be provide when using the word “data”. As …data were. This misuse of “data was “ occurs periodically throughout manuscript.

Pg 7. The method of preparation or ingredients of “conditioned” media should be indicated. Preparations of conditioned media vary among investigators.

Pg 8. Plural verb with “data” at two locations.

Pg 12. The compound “Q” has been introduced and repeatedly used throughout the manuscript. Although it has been presented in a previous publication, in
would be important for clarity and scientific comparison with the other organosulfur derivative that the structure be included in this manuscript. Preferably located in table 2 listing compounds examined in study.

Last paragraph: a “than” needs to added to the sentence. “…more potent than the parent structure”.

Pg 14. Identifying compound Q (cited at 2 locations) with its structure would help clarity of this section which compares the organosulfur compounds.

Pg 15. F1 has been listed here (1st line) as a member of group III compounds yet on previous page 12, it was listed as a group II compound. This needs clarification. Also, compound K was previously listed as a group II member on page 14 and, on page 15, it’s listed as a group III compound. Please clarify.

Compound Q again cited without access to molecular structure.

Last sentence of pg 15 should iterate the criteria assigned to each of the three groups.

Pg 16. Where Table 2 is indicated, do the authors mean Table 1 instead?

Should the term “metrics” or “matrix” be used?

Pg 19. Last paragraph should contain a listing for clarity of the18 compounds with their numbered subscripts.

H5 was indicated as displaying the most tumor-specific activity yet it was provided at the highest dose level (200 uM) than the other compounds. Should potency be based on mole per mole relationship or dose and time-dependency of exposure?

Pg 20. For consistency, “F” rather than “Q” should be cited as representing a compound that alters expression of a few genes. See page 15 where F was originally cited.

Pg 22. Regarding the proposed mechanism shown in scheme 3, would activity of the CC-linked alpha ester disulfide be compromised if catalase were introduced into the culture media?

Figure 1: legend should indicate which compounds are represented within each box in Fig 1A. Group III only shows presence of F6.

Figure 3 “Clusters” should be in the singular

Table 2: It would help clarity of the manuscript to include an additional column that shows which group each compound has been categorized.
Figure 3: Should depict on charts, the phases of the cell cycle indicated by percentage

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests with the publication of this reviewed manuscript.