Reviewer's report

**Title:** Methylation of WTH3, a Possible Drug Resistant Gene, Inhibits p53 Regulated Expression

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**Reviewer:** Volodymyr Tryndyak

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In this manuscript, entitled “Methylation of WTH3, a Possible Drug Resistant Gene, Inhibits p53 Regulated Expression”, by Kegui and co-authors evaluate the role of pigenetic mechanisms in regulation of WTH3 expression and its role in MDR development in tumor. The authors conclude that WTH3 plays an important role in MDR development and the transcription of WTH3 is regulated by DNA methylation and the p53 transcription factor.

This is a very interesting study. The question posed by the authors is well defined and the methods are appropriate and well described. The discussion and conclusions are also well balanced and adequately supported by the data. However, some issues with the manuscript need to be addressed.

1. What is 5-aza? Provide full name for this abbreviation.

2. In “Materials and methods” please indicate, what is IC50 of Dox for the MCF7/AdrR and MCF7/WT cell lines?

3. In addition of successful WTH3 knockdown shown by SQRT-PCR (Figure 3), I would recommend that authors do Western blot analysis or cytochemistry for MDR1 protein on HEK293 and MCF7/AdrR cell lines.

4. In the literature, there are a lot of data regarding promoter hypomethylation of genes that lead to gene overexpression and develop the multi-drug resistance in the tumor or decrease of apoptosis during cancer treatment. In view of this, authors must be cautious in their recommendation of restoring or increasing genes’ activity as a strategy for eradicating MDR encountered during cancer chemotherapy by introducing DNA demethylation reagents.

Finally, this manuscript can be accepted after minor essential revisions (which the authors can be trusted to make).