The manuscript entitled 'Methylation of WTH3, a Possible Drug Resistant Gene, Inhibits p53 Regulated Expression' and authored by Kegui Tian, Yuezeng Wang, Yu Huang, Boqiao Sun, Yuxin Li and Haopeng Xu describes the novel findings showing that over-expression of the WTH3 gene in multi-drug resistant (MDR) cells reduced MDR1 gene expression and converted their resistance to sensitivity to various anticancer drugs. Using the siRNA strategy to knockdown WTH3 expression, authors found that reduction in WTH3 levels resulted in increased MDR1 levels and elevated resistance to Doxorubicin. Authors also showed that DNA methylation adversely affected the positive impact of p53 on WTH3 promoter activity. These findings are important in the field of cancer research and provide new venues to understand the molecular mechanisms implicated in resistance to chemotherapeutic agents (e.g. doxorubicin, cisplatin, etc.) used in clinical practice.

1. The questions posed by the authors are well defined
2. The methods used are appropriate and very well described
3. The data are sound
4. The manuscript adheres to the relevant standards for reporting and data deposition
5. The discussion and conclusions are well balanced and adequately supported by the data
6. The limitations of the work are clearly stated
7. The authors clearly acknowledged any work upon which they are building, both published and unpublished
8. The title and abstract accurately convey what has been found
9. The writing is acceptable

I believe this is a solid work with important implications for cancer biology and pharmacology and I am suggesting the acceptance of this manuscript with minor essential revisions, which would include the correction of Fig.1A (upper panel should be redone to provide publication quality and avoiding vertical bar after sample"239-V"). There are several options to do so. Whether it is a combined gel that needed to be explicitly stated and respectively assembled with space or better to re-run another gel electrophoresis with all samples combined in one gel.
And make sure that a photograph presented shows in a right direction of electric field (seems that photograph of upper panel was accidentally reversed in vertical direction). Figure 2 requires standard deviation bars.