

## Peer Review File

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### Reviewer A:

**Comment 1:** since various metabolomic studies on ovarian cancer cells (sensitive and resistant) and their treatment with Pt-based compounds are available, is it possible to identify any relationship between what was reported in those studies and the role of KRT14? (see for example: Cells. 2024 Apr 9;13(8):661. doi: 10.3390/cells13080661.; Dalton Trans. 2022 Aug 23;51(33):12512-12523. doi: 10.1039/d2dt02068h.)

**Reply 1:** This is an excellent suggestion. Two studies indicate that some metabolites are altered in cisplatin-resistant A2780cis ovarian cancer cells compared to cisplatin-sensitive A2780 cells, suggesting that these metabolites may play a role in regulating ovarian cancer cell sensitivity to Pt-based compounds. We found that MATP, a gene that is significantly downregulated in KRT14-knockdown cells, is involved in cysteine and methionine metabolism, as well as metabolic pathways. This suggests that KRT14 may play a role in regulating metabolism, which could represent another molecular mechanism through which KRT14 contributes to cisplatin resistance. As a result, we have revised the discussion accordingly. Please let us know if you think any further modifications are necessary, and we would be happy to make additional revisions.

**Changes in the text:** Following sentences were added in discussion section: Some studies have reported differences in metabolite levels between cisplatin-sensitive and resistant ovarian cancer cell lines(21, 22). KEGG pathway analysis revealed that MATP, a gene that is significantly downregulated in KRT14-knockdown cells, is involved in cysteine and methionine metabolism, as well as metabolic pathways. This suggests that KRT14 may play a role in regulating metabolism, which could represent another molecular mechanism through which KRT14 contributes to cisplatin resistance (page 17 lines 308-313).

**Comment 2:** Explain “Three independent experiments were performed with three technical replicates”: does it mean a total of 9 experiments?

**Reply 2:** For qRT-PCR and Cell Counting Kit-8 assays, three technical replicates refer to setting up three wells for each independent experiment, with the goal of increasing the reliability and accuracy of the results. Both of these experiments were performed with three independent repetitions. For Hoechst 33258 staining, there is no three technical replicates for each independent experiment. We have revised test.

**Changes in the text:** we have modified our text as advised (see Page 10, line 165)

**Comment 3:** Throughout the text: IC<sub>50</sub> and not IC50.

**Reply 3:** There is no difference between IC<sub>50</sub> and IC50. Did you mean that I should change the "50" to a subscript?

**Changes in the text:** The IC50 in whole text have been changed into IC<sub>50</sub>.

**Reviewer B:**

1. Abstract

- It is needed to indicate the **aim** of the study in the Background.

**Response:** We changed the last sentence of background in abstract into "Therefore, this study aimed to explore the role and mechanisms of keratin 14 (KRT14) in regulating cisplatin resistance in ovarian cancer." If further revision is needed, please tell us.

2. Please also provide the full name of the abbreviated terms in the Highlight box.

**Response:** We have provided the full name of the abbreviated terms in the Highlight box.

3. Please check through your article to make sure **all** the abbreviated terms have been defined when they **FIRST** appear in the Abstract and the main text. "LRP11" "P-gp" "MRP1" in the abstract and "cDNA" "IgG-HRP" "FITC" "KEGG" "MATP" in the main text for example.

**Response:** We have provided the full name of above abbreviations. MATP should be MTAP, we have revised.

4. Please check the full name of "EP" "RIPA" in the text.

plasmid, termed as LRP11-OP. The transfection of si-NC, si-KRT14, empty plasmid pcDNA3.1 (EP),

Total cellular protein was extracted using radioimmunoprecipitation assay buffer (RIPA) buffer

**Response:** RIPA appeared only once, and we dropped the abbreviation. "EP" is correct.

5. For an Original Article, the main text should be structured as Introduction, Methods, Results, Discussion, and **Conclusions**. Please modify your article to it.

**Response:** We have modified our article according to your comments.

6. Figures and Table

- **All abbreviations** in figures/table and legends should be explained. "mRNA" in Figure 1 for example. Please check all abbreviations and provide the full names in the corresponding figure legend/table footnote.

**Response:** We have modified figure legend/table footnote according to your comments.

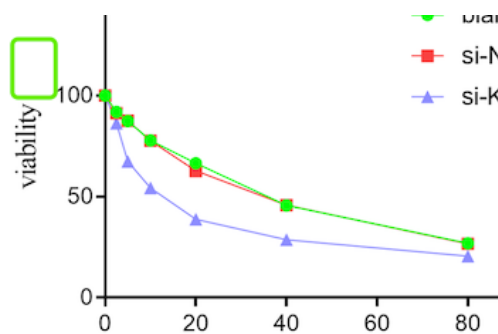
- Figure 2C, 2D; 5C, 5D: It is suggested to revise “SKOV3/DDP” to “SK-OV-3/DDP”, “A2780-DDP” to “A2780/DDP” to keep consistency.

SKOV3/DDP

A2780-DDP

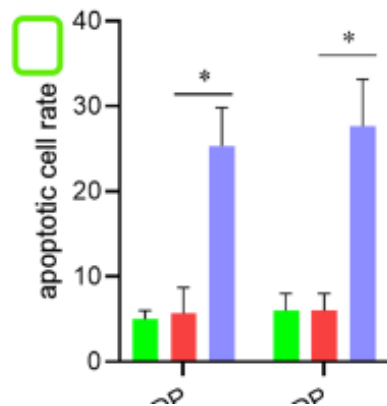
**Response:** We have modified Figure 2C, 2D; 5C, 5D.

- Figure 2C-D, 5C-D: Please check if unit (%) needed to add in each y-axis.



**Response:** Unit (%) is needed. We have added.

- Figure 3B, 6B: Please add unit (%) in the y-axis.



**Response:** Unit (%) has been added.

- Please indicate the magnification in Figure 3B and 6B legends.

**Response:** The magnification is 20×. We have added.

- Please indicate the meaning of the **arrows** in Figure 3B and 6B legends.

**Response:** The arrows indicate apoptotic cells. We have explained in the figure legends.

- There is no “MDR” in Figure 4, while it is explained in Figure 4 legend.

**Response:** We have deleted.

- Please double check Figure 4D legend.

“D: Western blot results for LRP11 expression in KRT14 knockdown cells.  
Right bar graph: KRT14 protein levels relative to GAPDH.”

**Response:** KRT14 should be LRP11. This sentence has been changed into ‘LRP11 protein levels relative to GAPDH.’

- Please double check the data in the following sentence.

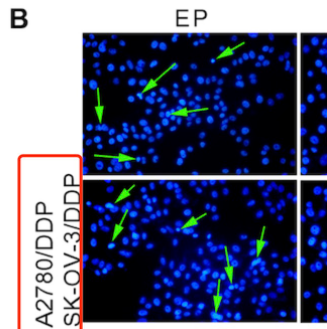
“In A2780/DDP cells, 221 mRNAs were up-regulated and 229 mRNAs were down-regulated under the same conditions (Figure 4A).”

**Response:** 221 should be 211. We have revised.

- There is no “IC<sub>50</sub>” in Figure 6, while it is explained in Figure 6 legend.

**Response:** We have deleted.

- Please double check Figure 6B.



**Response:** We have revised.

- Please submit Figure 3 and 6 in 2 versions: one version with the markers (arrows) and one **without**.

**Response:** We have provided 2 versions.