Dear Editors,

Thanks so much for your kind letter and the reviewers’ comments concerning the proof of our paper titled “The Effect of Ribosomal Protein S15a in Lung Adenocarcinoma” (#2015: 12: 8005: 0: 1: REVIEW). We have studied comments carefully and have made correction which we hope meet with approval. The revised portions were highlighted in the tracked changes version of our manuscript. The answers to the queries are provided as below:

Reviewer 1 (Anonymous)

Basic reporting

1. Line 261, where are the Figure 2E and 2F?

Answer: There are no Figure 2E and 2F.

Correction: Please remove the Figure 2E and 2F.

1. Line 301, Table 2 is the table 3.

Answer: Table 2 should be Table 3.

Correction: Please substitute “Table 2” with “Table 3”.

3. There are numerous grammatical errors throughout the text. For example, line 236 “Representative examplesof”, there was no blank between “examples” and “of”.

Answer: We have checked the manuscript carefully and made the correction of typo errors and grammatical errors.

Correction: The revised portions were highlighted in the tracked changes version.

Experimental design

Original primary research is appropriate within scope of the journal.

Validity of the findings

1. In the line 238, the criterion for calculating the immunopositive rates is not consistent. According to Table 1, the total number of cancer samples is not 75, but 80; however, the denominator used for the calculation is 75. In addition, why did authors not considered ‘+’ as immunopositive staining?

Answer: The total number of cancer samples is 75. We considered ‘+’ as immunonegative staining, because the immunopositive cells were still less than 15% of total cells in this group. To distinct the RPS15A overexpressed individuals, we considered ‘+’ as RPS15A mild positive and lower expressed group.

Correction: Please substitute ‘80’ with ‘75’.

2. In the line 250, authors determined the expression of RPS15 mRNA in several lung cancer cell lines, including H1299, A549, H1975, SK-MES-1, and H1688. Authors, however, only selected H1299 and A549 for subsequent studies; such as, in the Figure 2A, there was no expression level of H1975. Authors must provide the reason why they omitted H1975. Furthermore, why did authors choose H1299 in spite of its lowest level of expression?

Answer: We did not use the H1975 for this study, because this cell line was resistant to the lentiviral infection. Since lung adenocarcinoma is the most commonly diagnosed histological type of lung cancer, to investigate the role of RPS15A in lung adenocarcinoma, we choose H1299 and A549 cells for our study. RPS15A expression in H1299 cells was quite evident, when compared with GAPDH expression.

Correction: Please remove “H1975 cells”.

1. Statistical analysis should be included in Figure 3A and 3B.

Correction: Statistical analysis has been shown in Figure 3A and 3B.

4. Authors consistently provided both H1299 and A549 data. So, if possible, please provide key factors of p53 signaling pathway in H1299 cell in Figure 4E, too.

Answer: We performed western blotting assay of P53 signaling factors in A549 cells to confirm the result of gene profile microarray. As A549 was the only one cell line used to perform gene profile microarray, we did not perform the same experiment in H1299 cells.

Comments for the author

N/A

Reviewer 2 (Chengqi Xu)

Basic reporting

No Comments

Experimental design

No Comments

Validity of the findings

No Comments

Comments for the author

The whole of manuscript was well written, and the study was well designed. However, some issues need to be clarified as follows:

1.In figure 1A, what's the purpose that they detected the expression of RPS15A in these cell lines ? It makes no sense in this manuscript.

Answer: Since RPS15A was highly overexpressed in cancer tissue samples, we detected the fundamental expression level of RPS15A in lung cancer cell lines to see if it was consistent with our findings. Additionally, the determination of RPS15A expression level in cancer cells provided a significant clue for lentivirus design.

2.In the Results, the authors mentioned that RPS15A is obviously expressed in lung cancer cell lines. The authors should compare the expression of RPS15A in lung cancer cells to normal lung cells, in order to suggest whether the RPS15A is overexpressed or underexpressed compared to normal cells. These information can be important in the further clinical application.

Answer: We have compared the RPS15A level between cancer samples and adjacent normal tissue samples. RPS15A was greatly overexpressed in cancer samples, when compared with that of normal tissue.

3. In figure 3c, the quality of the colony formation assay is poor. No obvious colonies are showed, and they are not supposed to be concentrated in the central area.

Answer: We improved the image quality.

4. The figure legends lack necessary details to fully understand the figures. A more comprehensive figure legends is needed.

Answer: We checked figure legends carefully and made some revisions.

Correction: The revised portions were highlighted in the tracked changes version.

5. There is typos and grammatical errors in the manuscript. Overall, the manuscript needs proofreading and polishing of the language.

Answer: We have checked the manuscript carefully and revised typo errors and grammatical errors.

Correction: The revised portions were highlighted in the tracked changes version.

We greatly appreciate the efficient, professional and rapid processing of our paper by your team. If there is anything else we should do, please do not hesitate to let us know.

Special thanks to you for your good comments.
Best regards.

Sincerely yours,

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