

**UC San Diego**  
Jacobs School of Engineering

Shicheng Guo <shg047@eng.ucsd.edu>

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## Receipt of reviewer's report for SREP-16-02746

1 message

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**scientificreports@nature.com** <scientificreports@nature.com>  
Reply-To: scientificreports@nature.com  
To: scguo@ucsd.edu

Sat, Feb 27, 2016 at 4:31 PM

Dear Dr Guo,

Many thanks for submitting your referee report on "Prediction of the prognostic value of Beclin1 in human non-small cell lung cancer via combined analysis of protein and mRNA expression" by Dr Wu. We appreciate the time you have taken to review this manuscript for Scientific Reports. A copy of this report is attached below for your reference.

Best regards,

Manuscript Administration  
Scientific Reports  
4 Crinan Street  
London N1 9XW  
E-mail: [scientificreports@nature.com](mailto:scientificreports@nature.com)

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Is the manuscript technically sound?: No

Could the manuscript become technically sound with revision?: Yes

Are the conclusions supported by the evidence presented?: No

Are additional experiments or data required to support the conclusions?: Yes

Does the manuscript only duplicate previous work?: No

Appropriate use of statistics and treatment of uncertainties?: No

References: appropriate credit given to previous work?: Yes

Is the manuscript written clearly using Standard English?: Yes

Electrophoretic gels and blots are presented clearly and are free from apparent manipulation?: N/A

Technical Comments to the Author:

Recommendation: Major Revision

Remarks to the Editor:

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Comments to the Authors,

Dr. Xia provided an integrative analysis to the prognostic value of Beclin1 in human non-small cell lung cancer from protein and mRNA levels. The idea and the strategy were excellent and it would give a great help to understand the relationship between Beclin1 and the outcome of lung cancer. However, I have several considerations on the study design and the statistical method.

1, In the section of the meta-analysis based on Beclin1 protein, the conclusion of the meta-analysis would be suspected since only 5 literatures were enrolled, meanwhile, the samples were only from East Asian (China and Korean). The bias conclusion would be obtained because of the locally sampling.

2, Authors mentioned 704 patients from 5 studies were enrolled, however, Figure 1 shown there are only 599 patients from 4 studies. Again, the author mentioned "included five prospective studies with 703 NSCLC patients in our meta-analysis", why these numbers were changed again and again?

3, For the result section, the sub-title should be sentence with specific conclusion rather than "Protein analysis", "mRNA analysis".

4, In the section of the mRNA analysis based on TCGA dataset, how did the author extract the "overall survival" information from TCGA database? As I know, no such information was collected by TCGA project. The authors collected the information directly or inferred the "overall survival" by other information? If the author inferred "overall survival", then the method should be provided. In addition, in a nonrandomized clinical trial or an observational study, the samples in different groups may be biased due to some confounding variables, hence the Kaplan-Meier estimator is inappropriate. When confounders are present, survival function estimates can be adjusted and compared.

5, In Figure 4, what's the value indicated should be mentioned and the method was invited by the author or not? If it is not originally invited by the author, then the software or the algorithm should be cited.

6, what does "The positive control was SPP1(OPN) which was reported by Zou XL 32" mean? Any special role for this control? How to use this control?

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