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## Final Decision made 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

Mon, Feb 29, 2016 at 8:12 AM

Dear Dr Guo:

Thank you for your help with manuscript SREP-16-02746, "Prediction of the prognostic value of Beclin1 in human non-small cell lung cancer via combined analysis of protein and mRNA expression", which you recently reviewed for Scientific Reports.

For your records, the decision for this manuscript, based partly on your input, was Reject. A full copy of the comments to authors is appended, below.

Your assistance and participation in the review process for Scientific Reports is greatly appreciated.

Best regards,

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Scientific Reports  
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Referee comments to the authors:

Reviewer #1:

Remarks to the Author:

In the current study, the authors aim to develop a new approach to access the predictive value of Beclin1 in human NSCLC from both protein and mRNA level by the method of meta-analysis. Only 703 protein data and 783 mRNA expression data were included in the current study. They found Beclin1 protein is a useful indicator for the outcome prediction of NSCLC.

Several flaws should be addressed.

1. The current meta-analysis was based on limited sample size which may have limited statistical power.
2. I do not think the current study add anything new to this area.
3. In the Title page, the authors should pay attention to the consistence and spelling.
4. The authors should follow the reference style of Scientific Reports.
5. The authors only search publications from PUBMED and EMBASE, and may miss lots of publications such as written in Chinese.
6. Only five studies were included in the current meta-analysis, that is a far way to perform meta-analysis, the authors should use their own data besides the data from others.
7. As the authors provided, "significant heterogeneity among studies was observed ( $I^2=72.50\%$ ,  $p=0.006$ )," think about the heterogeneity and limited sample size as well as limited study number, the conclusions were doubtful.
8. The authors should calculate the statistical power.
9. The authors should perform FPRP analysis to avoid false positive findings.

Reviewer #2:

Remarks to the Author:  
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 used by the author or not? If it is not originally used 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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