Reviewer’s report

Title: Prognostic implications of ezrin and phosphorylated ezrin expression in non-small cell lung cancer

Version: 1  Date: 9 December 2013

Reviewer: Elvira Stacher

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The study presented by Jin et al elucidates the expression patterns of total ezrin and two phosphorylated sites in NSCLC. The expression patterns are correlated with clinical and pathological parameters. Overall, the study is scientifically sound and contributes to the understanding of the potential role of this particular protein in lung cancer. However, the paper needs amendments in order to be considered for acceptance.

Major compulsory revisions:
1. Page 12-16:
The discussion needs to be rewritten. It is just a summary of the existing literature and therefore very exhausting to read. How do you explain that total ezrin staining can be lower than p-ezrin staining? Please also comment on already known mutations in NSCLC (especially in adenocarcinomas) and their potential interaction with ezrin.

Minor essential revisions:
1. Page 2 (Conclusions Abstract): Omit first sentence since this statement is completely overdrawn.
2. Page 5: Specify accurately how samples were examined. Was it a tissue microarray? If yes, how many punches per tumor? How many punches per healthy tissue?
3. Page 6:
Please provide a table for this paragraph to sum up the patients’ characteristics.
Age and gender (although I believe the term sex should be used since it refers to the biological state) are biological or clinical parameters, the remaining ones pathological. Were all tumors untreated prior to surgery? In adenocarcinomas, is there a link with EML4/ALK or EGFR-mutation status? Is there any correlation with histological subtype (acinar, micropapillary, mucinous,…)?
Omit the word “carefully”.
Specify „follow-up deadline“ and provide a time range for the follow-up period.
How many deaths were not attributable to the malignant condition? Please explain – what was the cause in the remaining cases?
How were discrepancies between these two pathologists resolved?
4. Page 7:
Please provide information regarding the specificity of the antibodies used.
Regarding the immunohistochemical staining: I understand that the scoring applied refers to the number of stained cells. Did you take the intensity of the staining into account?

5. Page 9:
Spelling mistake: cytoplasmic
Which structures (pneumocytes, endothelial cells, respiratory epithelium,…….) were stained in non-tumor tissue? Were macrophages included in the scoring? How do you explain the difference between the staining patterns of adjacent and normal lung tissues?

6. Tables 1 and 2:
The P-value is capitalized and has to be in Italics. Please keep the P-value consistent in the main text and the tables (either with or without a zero before the comma, check with the journal’s policies).

7. Table 2:
Differentiation (parameters in the table): it should read „well-moderate-poor“
Last line: it should read „poorly vs well and moderately differentiated tumors“

8. Figure 1:
Provide a picture of positively stained normal lung tissue (either adjacent or of controls).

9. Figure 2:
Provide P-values.

10. Figure 3 and 4:
The resolution is not acceptable. Redo both figures.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests.