Reviewer’s report

Title: Overexpression of NIMA-related kinase 2 is associated with progression and poor prognosis of prostate cancer

Version: 2 Date: 2 April 2015

Reviewer: Michael Schweizer

Reviewer’s report:

The authors present interesting data regarding the potential role that NEK2 plays in promoting prostate cancer cellular proliferation, disease progression and its association with pathologic features. Some details regarding the presented analyses are not included and a few of the conclusions are not substantiated by the presented experiments. Specific comments are below:

Major Revisions:

1. The introduction and discussion section need to be toned down a bit. While NEK2 may prove to be a good biomarker, this data presented in this paper is preliminary in nature and needs to be confirmed in prospectively collected human specimens. This should be addressed in the discussion. Statements similar to “…overexpressed NEK2 is of prognosis value for predicting outcome of PCa recurrence” should be reworded so as to not be so definitive.

2. How was PSA recurrence defined? Clarify how overall survival was defined. What does ‘death other than unexpected causes’ mean? Is this cancer-specific deaths? If so, you are not measuring overall survival, but rather cancer-specific survival.

3. For the IHC analyses, why wasn’t percentage of positive cells considered on a continuous basis when generating the IRS score? There is no need to categorize the percentage of positive cells.

4. Please provide P-values for the following figures: Fig 1a, Fig 1d, Fig 2c

5. Regarding the discussion of fig 2a, avoid using conjecture. If you believe that NEK2 knockdown results in compromised angiogenesis, you should present objective data regarding the vascularity of each tumor.

6. Regarding the discussion for Fig 2d-e, provide the mean IRS score for NEK2 knockdown vs control xenografts with P-values. For the fig 2 legend, remove the statement that ‘NEK2 expression is obviously downregulated’.

7. In Fig2d-e, it is unclear what you are trying to convey when you state “NEK2 protein are mainly localized at the nucleus and cytosol”. Where else would NEK2 expression be observed? Is there evidence that NEK2 is secreted from cells? Why would siRNA knockdown of NEK2 affect its cellular localization?
8. You indicate in the discussion that NEK2 can drive drug resistance. What is the purposed mechanism behind this effect? Is there any evidence for this in prostate cancer? I would evaluate the effect of NEK2 knockdown on drug resistance if you think it plays a role in promoting prostate cancer drug resistance.

Minor Revisions:

1. There are awkwardly worded phrases throughout the manuscript. For instance, the word ‘the’ is used inappropriately in multiple places (e.g. ‘the chemotherapy’, ‘post the surgery’, etc.). Would proof read the article again for grammar.

2. The legend for Fig 2c should read ‘Scr’ not ‘Src’. Please correct this.

3. For Fig3c, did you mean to indicate that this is a sample of Gleason >8 or #8?

4. For the Fig 4a-b, you should provide a table below each KM plot to indicate the number of at risk patients at each time point.

5. I assume that in Fig 4 a log-rank test was used. Indicate this in the ‘statistical analysis’ section of the manuscript.

6. There are several statements in the discussion that require a reference. Please provide references for the sentences beginning on lines: 234, 235 and 250.

Discretionary Revisions:

None.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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.