**Reviewer’s report**

**Title:** Eukaryotic Elongation Factor-2 Kinase Expression is an Independent Prognostic Factor in Colorectal Cancer

**Version:** 1  **Date:** 29 Mar 2019

**Reviewer:** Veronique Giroux

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BCAN-D-19-00327R1

Eukaryotic Elongation Factor-2 Kinase expression is an independent prognostic factor in colorectal cancer

The authors and other have previously shown that EEF2K could act as a tumor suppressor in colorectal cancer using cell lines and in vivo models. Herein, they have performed some expression experiments and clinical data analysis to suggest that EEF2K expression could be used as a prognostic factor. They have used several approaches that all lead to the same conclusions. Overall, it is a well-conducted study that suggests a new prognostic tool for colorectal cancer. However, further in-depth analysis would strengthen the manuscript.

Major comments:

1. Since colorectal cancer exists in several different types (sporadic vs hereditary; adenocarcinoma vs serrated vs …), more information regarding the tissues used for the expression experiments would provide insightful data. Also, does EEF2K expression correlate with any subtypes of colorectal cancer?

2. Figure 1C: Is there anything common between the 5 samples that did not show a decrease in EEF2K expression? Subtypes, mutation, localization, differentiation status, treatment regimen, etc.

3. Due to the published role of EEF2K in cell proliferation of APC-deficient enterocytes, is there any correlation between EEF2K expression and APC mutation status in their samples as well as TCGA data? Any correlation with other common mutations (TP53, KRAS, SMAD4, MSI vs MSS)

4. Due to the relation between EEF2K and chemotherapy response, is there any correlation between EEF2K expression and previous cancer treatments in the patients analyzed (naïve vs chemo-treated) in their own cohort as well as TCGA data?

Minor comments:
5. Page 4, line 75: should read as "up to 50% patients whom underwent"

6. Page 5, top paragraph: some references should be included to support that the clinical value system currently in used could be improved to better pinpoint the best treatment for the different patients

7. Page 9, line 169: What was the cut-off value (intensity and/or percentage of stained cells) used to delineate positive vs negative expression?

8. Page 11, line 198: should read as "subjected"

9. Page 13, top paragraph, last sentence: Sentence should be revised to make it clearer.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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