Peer Review File

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Reviewer Comments

The MS of Zhou et al. incorporates sophisticated extraction pan-genome data (transcriptome alterations in ACC tumor cases), and several years of Xiangya Hospital cohort patient specimens in correlation with clinical data, to evaluate KIF 11 as a prospective prognostic marker and its therapeutic implications. Available cell lines do not reflect ACC heterogeneity and specific therapeutic responses of individual patients, so data analysis-sequenced clinical cases are very significant.

Suggestions for improvements:
Line 33 suggests that a lab method platform was used, whereas in this case it was bioinformatic data analysis. '…KIF11 expression in ACC and normal tissues was determined using The Cancer Genome Atlas'… would be better expressed as it is in the sentence 'The Cancer Genome Atlas (TCGA) database (n = 77) and Genotype Tissue Expression (GTEx) database (n = 128) were utilized' … (line 94-96)
Answer: Thank you for your valuable advice, we have modified our text as advised (see Page 1-2, line 33-35).

Lines 42 and 43 I suggest '…and associated with the T, M, and pathological stages, primary therapy outcomes….be changed to '…associated with T (primary tumor), and M (metastasis) and stages of tumor progression. (First use of an abbreviation should be explained in brackets if it is not in the abbreviation list).
Answer: Thank you for your important comments, we have modified our text as advised (see Page 2, line 42-43).

Method paragraph 'Differential expression of KIF11; TCGA and GTEx database analyses'
The TCGA database is a collaborative research network effort to make whole genomic cancer data available, in order to move forward cancer diagnosis, prevention, and treatment. A unified effort involving data access, data extraction and bioinformatic analysis is a challenge. Zhou et al.'s work is significant as it gives an example of how to use the database and it propagates awareness of the role of this unified network structure in cancer discoveries.
More about data types taken from the database should be added. It's not clear whether the differential expression data given is based on large-scale protein array or RNA seq. (This ref may be helpful: Tomczak, Katarzyna, Patrycja Czerwińska, and Maciej Wiznerowicz. Review The Cancer Genome Atlas (TCGA): an immeasurable source of knowledge. Contemporary

Oncology/Współczesna Onkologia 2015.1 (2015): 68-77). This database for readers mostly emphasises genomic data, while proteomic data based on high sensitivity protein array is less prominent, so it is important to specify which was used.

Answer: Thank you for your important suggestions. Our data is RNA seq data that comes from TCGA and GTEx database in transcripts per million reads (TPM) format, which are uniformly processed by Toil process [(1).] We have modified our text as advised (see Page 4, line 96-98).

（1）Vivian J, Rao AA, Nothaft FA, et al. Toil enables reproducible, open source, big biomedical data analyses. Nat Biotechnol 2017;35:314-6.

RNA-seq and microarray analysis is mentioned for the first time in the discussion at line 346. This should be described in the method section as noted above. Which approach is used can be a source of bias. Gene set enrichment analysis is different for microarray and RNA-seq data and so can also be a source of bias.

Answer: Thank you for your important comments. It should be RNA-seq analysis, we have modified our text as advised (see Page 12, line 347).

Protein names are conventionally written in written normal script and a gene names in cursive, which is needed to make clear when protein or gene expression level is being referred to.

Answer: Thank you for your important comments, we have confirmed it.

The passage starting at line 206 is not quite clear and there is some repetition. I suggest a rewrite as follows:

Furthermore, IHC staining to detect KIF11 expression showed that it was significantly higher in ACC samples than in normal adrenal tissues (Figure 2B, 2C). The staining intensity was divided into 'KIF11-high' (≥ 30% positive nuclei) and 'KIF11 low' (<30%positive nuclei) groups, for comparison with clinical severity (given below).

Answer: Thank you for your important suggestions, we have modified our text as advised (see Page 8, line 208-212).

Referring to the paragraph starting from line 332 about KIF11 therapeutic potential, have there been any clinical research studies on KIF11 inhibitor published on clinical.trial.gov? If any, it would be valuable to add this.

Answer: Thank you for your valuable advice, we added the clinical research studies of KIF11 inhibitor (published on clinical.trial.gov) in the discussion section (see Page 8, line 339-341).

line 234 Spearman

Answer: Thank you for your important comments, we have modified our text as advised (see Page 8, line 235).

line 500 (Fig 3 legend) correlated

Answer: Thank you for your important comments, we have modified our text as advised (see Page 16, line 502).