

This work by Bu L, Huang F et al. attempts at identifying a vitamin D-related gene signature to predict prognosis in colorectal cancer (CRC) patients. The authors have screened close to 200 genes with regard to patient information obtained from The Cancer Genome Atlas (TCGA) and narrowed down to a novel 17-gene signature. The signature is then tested on one external dataset from GEO to validate the findings. The authors built a nomogram to revalidate their findings from previous analysis.

The reviewer feels that the work lacks novelty since similar attempts at identifying signatures have been performed previously. Moreover, a number of concerns ranging from lack of rigor in experimental design to overstatement of findings to poor quality of writing makes the manuscript poor. A resubmission after improvements is recommended.

The major concerns are listed below:

1. Since this is an analysis-heavy article, authors should explicitly provide every possible detail of how various analyses were done. In this regard, the materials and methods (M&M) section needs to be majorly revamped and rewritten.
2. Details about the input FPKM data is missing. As a rule of thumb, FPKM cannot be used for comparison of gene expression between samples. Did the authors perform normalization of gene expression using a standard tool? If not, that's a good start point. There is inconsistency in the number of samples analyzed. The number changes from 480 CRC patients to 393 and 630 patients along the manuscript. The variation in numbers is difficult to follow. All such details should be added to the M&M section.
3. Similarly details about parameters used for various analyses and R packages should be added. The reviewer believes that this is absolutely necessary since the results and conclusions are derived purely from bioinformatic analysis using R packages.
4. The writing is poor and incoherent which further makes it difficult to follow what the authors want to convey. For example, lines 110-114 repeat the same conclusion as in lines 104-106. There are similar instances throughout the article.
5. Calculation of risk score shown in lines 117-122 needs to be in M&M. The source of numbers used for calculations is not explained.
6. Figure and table legends should be more explanatory. Figures are zoomed-in and blurry.
7. Results in figure 6 should be explained in text. This will increase impact of the findings.
8. The reviewer feels that using only one testing set from GEO (GSE17536) is not enough to assert the validation of the findings. More datasets with variable patient number would give robustness to the conclusion. At this point, the conclusion is overstated.