

## Basic reporting

1. Figure legends for the supplementary figures are missing.
2. Line98-99, how were the coefficients for each gene computed? Providing more information for clarity. Also elaborate on how a concordance index is used to discriminate and calibrate nomograms in the methods (Line109-110). The global p value for the best model shown in Fig2b should also be reported.
3. In Figure3, the survival plot figures should include more description, for example, what is the median survival for high risk and low risk?
4. Line113-114, and Line187, what is specifically the statistical test used to for the pathway analysis? Is it over-representation analysis or gene set enrichment analysis? Need to specify. Also it would be interesting to report what genes/gene sets are altered in expression that led to the altered pathway activity. Were any of the four genes in the signature in any of these significant pathways?
5. The figure5 needs to show the statistical test used in each case and the number of samples in each group.
6. How were the columns of Fig6A ordered? Was it ordered randomly or based on the low/high risk group?
7. The author should elaborate on the interpretation of nomogram and how it can be used to predict the survival of patients.
8. The r packages used for the analysis should also be cited, such as "rms", "clusterProfiler", "corrplot", etc.

## Experimental design

1. In this study the authors did a very nice study of breast cancer prognostic biomarker discovery. They first identified genes that are differentially expressed between resistant cell lines and parental cell lines and then they established a link between these genes and survival probability of patients who are ER+ and HER2- . They demonstrated the independent prognostic value of the four-gene based signature and constructed comprehensive models to predict patients DFS. Very well done overall.

### **Validity of the findings**

1. For the results presented in Fig6 B, since there are multiple tests for significance, are the P values reported after correction for multiple-testing? It is not mentioned in the body of the text nor legend.
2. In the multivariate models Fig7 b and Fig7 C, the relative importance of each variable is different, can the authors explain the discrepancy? Also what is the statistical test used to calculate the p values?

### **General comments for the author**

1. Overall very nice work. Just need to add more description to the figure legends and methods section as suggested above, as well as adding legends for supplementary figures.