Peer Review File

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Reviewer A

Overview:

Comment 1: The authors mentioned an important aspect of early-stage breast cancer in the background of the abstract but did not state it in the part of the introduction. Moreover, the authors emphasize the recurrence of breast cancer. Therefore, could the authors rearrange them together?

Reply 1: we have rearranged them together as advised.

Changes in the text: see Page 2, line 21-24; Page 4, line 61-76

Comment 2: It would be perfect if the authors provided information on the sensitivity and specificity of this prognostic model, both in the abstract and the results, and discussed in brief in the part of discussion.

Reply 2: we have provided information on the sensitivity and specificity of this prognostic model, both in the abstract and the results, and discussed in brief in the part of discussion.

Changes in the text: see Page 2-3, line 40-42, Page 11-12, line 228-232, Page 12, line 239-243, Page 17, line 353-360.

Comment 3: The authors explained that 15 prognostic-related genes were screened for constructing a prognostic model, but only 14 genes were mentioned in the qPCR analysis. Moreover, only 13 genes were reported in Figure 9. Therefore, it would be nice if the authors explained why these genes were lost in the study.

Reply 3: we have explained why these genes were lost in the study.

Changes in the text: see Page 9, line 183-188

Comment 4: The names of genes should be in italics.

Reply 4: We italicized all the gene names in the text.

Changes in the text: see Page 9, line 183-186; Page 11, line 222-227; line 265-266; Page 13, line 270; Page 15, line 313-315; Page 17, line 361, Page 18, line 368-377, Page 19, line 391. Table 1, Table 2.

Introduction:

Comment 5: It would be perfect if the authors emphasized how the prognostic model and molecular mechanism pathway are important to breast cancer management in the part of the introduction.

Reply 5: We emphasized how the prognostic model and molecular mechanism pathway are important to breast cancer management.

Changes in the text: see Page 5, line 79-82.

Comment 6: Lines 42-45: Gene mutation is referred to as a genetic factor; therefore, the authors should describe it together.

Reply 6: we have modified our text as advised.

Changes in the text: see Page 4, line 59.

Materials and Methods:

Comment 7: The name of the company is required for chemicals and instruments.

Reply 7: we have modified our text as advised.

Changes in the text: see Page 9, line 177-186.

Comment 8: More details are needed for both normal and tumor breast tissues, which were used in qPCR analysis.

Reply 8: we have modified our text as advised.

Changes in the text: see Page 9, line 171-173.

Comment 9: Line 88: The sub-topic should be in bold.

Reply 9: we have modified our text as advised.

Changes in the text: see Page 6, line 102.

Comment 10: Line 147: The sentence needs a capital letter.

Reply 10: we have modified this sentence.

Changes in the text: see Page 8, line 155

Result:

Comment 11: Line 194: There is a typing error since there are two green.

Reply 11: we have modified our text as advised.

Changes in the text: see Page 10, line 205.

Comment 12: Figures 5A and 5B do not mention in the content (sub-topic: Impact of Risk Scores on Tumor Microenvironment and Immune Cell Dynamics).

Reply 12: We have added some descriptions about Figures 5A and 5B.

Changes in the text: see Page 13, line 253-259.

Comment 13: Figure 5D has two panels; therefore, please add information to describe the top panel and the panel below in the figure or in the figure legend.

Reply 13: We add information to describe the top panel and the panel below in the figure legend.

Changes in the text: see figures profile, figure 5D legend.

Comment 14: Line 282: There are typing errors in the words "GVSA and GESA".

Reply 14: we have modified our text as advised.

Changes in the text: see Page 14, line 287.

Comment 15: Lines 284–287: It seems the sentence is ambiguous; therefore, could the authors re-examine for grammar?

Reply 15: we have modified our text as advised.

Changes in the text: see Page 14, line 289-292.

Comment 16: Line 315: Should be specific to Figures 9A and 9B.

Reply 16: we have modified our text as advised.

Changes in the text: see Page 15, line 316.

Discussion:

Comment 17: The full term is needed for the abbreviation of "PRS".

Reply 17: we have modified our text as advised.

Changes in the text: see Page 17, line 341.

Comment 18: It would be nice for the reader if the authors provided more discussion on gene functions and their signaling pathways of the three prognostic-related genes, i.e., SPINT1, EZR, and SIAH2, which were increased significantly in clinical BRCA samples compared with the normal group.

Reply 18: We have added some descriptions about the related genes.

Changes in the text: see Page 18-19, line 361-387.

Comment 19: Ethics statement: Need to provide the ethical approval number and year of approval.

Reply 19: we have modified our text as advised.

Changes in the text: see Page 20, line 408-409.

Reviewer B

Please check if the “>” should be “≥” in the following sentence.

Reply (1): we have modified our text as advised.

Changes in the text: see Page 12, line 239.

Please unify the CD8+ and CD8 in your figures and main text.

Reply (5): we have modified our text as advised.

Changes in the text: see Page 13, line 264.

Is any description needed for the axes of the following part in Figure 5D?

Reply (6): we have modified both our text and Figure 5D as advised.

Changes in the text: see Page 13, line 276.

Please modify the P values in the main text and figures.

Reply (3): we have modified the P values in Figure 5E and Figure 6 as advised.