

## Peer Review File

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### Reviewer Comments

The development of transcriptomics allowed to provide a new perspective of understanding the carcinogenic process. However, the function of several lncRNAs has remained unknown. The present study aimed to evaluate the expression of lncRNA LINC02613 in breast cancer, investigating its relationship with clinicopathological characteristics. For this, the authors used data from the TCGA. Overall, low LINC02613 expression was associated with ethnicity, mean age, pathological stage, TNM classification, and expression of immunohistochemical markers (ER, PR, HER2). Furthermore, low expression of LINC02613 was predictive of low overall survival.

Below are some suggested corrections and changes for the authors:

In the abstract I suggest that the authors better describe the results of the study. The information provided is very vague "Low expression of LINC02613 was associated with ethnicity, mean age, pathological stage, T&N stage and expression of immunohistochemical markers (ER, PR and HER2)."

Reply: We have reviewed and corrected the statement. (see line 40-42)

Changes in the text: Statistical analysis revealed that low expression of LINC02613 was associated with Asian ethnicity, older age, higher histological grade, and higher expression of ER, PR and HER2.

### Introduction

Lines 52-54 - The authors claim that the breast cancer rate in China has been increasing at a rate of 3-5% annually, but the reference provided is for 2005. I believe this data is outdated.

Reply: We have reviewed the relevant epidemiological data and made new statements. (see line 62-63)

Changes in the text: From 2017-2019, China was one of the top 3 countries in the world with the most breast cancer incidence and death.[2, 3]

### Materials and Methods

Line 112 – Reference 16 (Gabriela Bindea et al.) is not the one described in the references at the end of the manuscript. I believe it is missing.

Reply: We have searched and corrected the relevant reference. (see line 615)

Changes in the text: Bindea G, Mlecnik B, Tosolini M, Kirilovsky A, Waldner M, Obenauf AC, Angell H, Fredriksen T, Lafontaine L, Berger A et al: Spatiotemporal dynamics of intratumoral immune cells reveal the immune landscape in human cancer. *Immunity* 2013, 39(4):782-795.

## Results

Lines 141-151 - Provide the number of each of the analyzed tumor subtypes.

Reply: The number of tumor subtypes has been provided. (see line 164)

Changes in the text: After preliminary analysis, LINC02613 was found to be lowly expressed in 24 tumor subtypes including...

Lines 161-162 – “including 60 Asian patients and 916 non-Asian patients (179 black or African American patients and 737 white patients).” The authors separate the patients into Asians and non-Asians. It is not clear why this is. Patients should be separated into Asian, Black or African American and White. It is known that breast tumors in black patients may have a worse prognosis, or even more aggressive tumor subtypes.

Reply: We have reclassified race and renewed Table 1 and corresponding conclusions. (see line 416 Table 1 and line 189-191)

Changes in the text: Statistical results showed that a greater proportion of Asian patients expressed low LINC02613 compared with others. ( $p=0.006$ ).

Lines 168-169 – “In addition, we noticed more patients with lower expression of LINC02613 in T4 and non-N0 stages...”. As mentioned above, the distribution of tumors in T4 and non-T4 does not make sense. The authors should divide the tumors into T1-T2 and T3-T4.

Reply: We divided tumors into T1, T2, T3, T4 for T stage and N0, N1, N2 for N stage respectively. (see line 197-198 and line 495 Table 1)

Changes in the text: In addition, we noticed more patients with low expression of LINC02613 in the T4 stage and N2 stage respectively (71.4% for T4,  $p=0.04$  and 63.8% for N2,  $p=0.01$ ).

Figure 4 can be added as a supplement. The information contained therein is the same as in Table 1 but represented in a different way.

Reply: Thank you for your suggestion and the changes have been made.

Changes in the text:

Lines 181-182 – “Kaplan-Meier analysis revealed that in all patients, low expression of LINC02613 was associated with poor OS (HR=0.65 (0.49-0.90),  $P=0.01$ ) but had nothing to do with DSS and PFS.” Rewrite this sentence. The expression in the English language was not good.

Reply: We have reviewed and rewrote the sentence. (see line 210-211)

Changes in the text: Kaplan-Meier analysis revealed that low expression of LINC02613, although having no effect on DSS and PFS, predicted worse OS in patients (HR=0.65 (0.49-0.90),  $P=0.01$ )

Lines 183-185 – “Further subgroup analysis revealed that low LINC02613 expression was significantly associated with poor OS of patients in stage T2 (HR=0.581 (0.364-0.928),  $P=0.023$ ), stage N0...” It is not clear why the authors only detailed these cases. Was an individual assessment performed for all variables and only these were significant?

Reply: Individual assessments were performed for all TNM variables and only these were

statistically significant. We reconsidered and decided to present this result in the form of a forest plot. (see line 512, Figure 5)

Changes in the text: Subgroup analysis for TNM stage system revealed that low LINC02613 expression was significantly associated with poor OS of patients in stage T2 (HR=0.581 (0.364-0.928),  $P=0.023$ ), stage N0 (HR=0.540 (0.297-0.982),  $P=0.043$ ) and stage M0 (HR=0.660 (0.459-0.949),  $P=0.025$ ) (Fig. 5).

Figure 7 – Check the subtitle. “Row 9-11 shows corresponding...”

Reply: The error has been fixed.

Changes in the text: Row 9-11 shows corresponding survival probability

Figure 10, 11 and 12 can be included as supplementary material.

Reply: Thank you for your suggestion and the changes have been made.

Changes in the text:

Note: Check English. There are many prepositions and some expressions that can be improved.

Reply: The language has been checked and some appropriate changes have been made.

Changes in the text: