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CORRESPONDENCE

Correspondence (reply): The application conditions of false discovery rate control

We have carefully read the correspondence "False Discovery Rate Control in Cancer Biomarker Selection" authored by Li. The author clarified the need of paying attention to the control of false discovery rate (FDR) when screening for cancer biomarkers. They expressed concerns about whether the 30 genes concluded in Figure 7 in our published paper "LPCAT1 functions as a novel prognostic molecular marker in hepatocellular carcinoma" call for FDR control.[1] We would like to express our great gratitude to the author for his attention to the article published by our team. The questions raised by the author allowed us to deeply look into clinically relevant statistical issues. We would like to make the following explanations.

First of all, please let me explain the source of those 30 genes. We first screened out differentially expressed genes in each group with *P* value ($P < 0.05$) and FDR ($P < 0.05$) as cutoff, and obtained 1314 overlapped oncogenes related to lysophosphatidylcholine acyltransferase 1 (LPCAT1). Then, the Kaplan Meier plotter analysis was performed on those 1 314 genes for the 5-year survival of hepatocellular carcinoma (HCC) and finalized on the top 30 most related to LPCAT1.

FDR is a commonly used false positive control method in multiple hypothesis tests.[2] Rather than completely avoid the false positive results, this method aims to restrict the proportion of false positive results and true positive results within a certain range. Multiple-test means multiple hypothesis test conductions. Every hypothesis test comes with risks, and when the null hypothesis is rejected, we tend to commit type I errors (false positive errors). In a single hypothesis test, the significance level or type I error rate for a single test is the calculated *P* value. However, when hypothesis testing is used multiple times to answer the same question, the chances of type I error increase, elevating the false positive rate. Hence, false positive rates are in need of regulation when a clinical trial involves multiple indicators or intergroup analysis and requires multiple-test.

Second, FDR is one method of adjusting the *P* value in multiple hypothesis tests to avoid type I errors (false positive errors) caused by numerous tests. In other words, multiplicity is the prerequisite for FDR. A clinical trial involving multiple factors requires multiple times of hypothesis testing, where FDR is required for adjustment of the *P* value. When the comparison was conducted between two groups, with a 5-year survival rate as the only indicator, multiplicity should no longer be regarded as an issue. The Kaplan–Meier plotter curve in Figure 7 showed the 5-year survival rates between the two groups separately. The influence of each gene on the survival is independent of one another. Given only one hypothesis test was conducted in the process of statistical analysis, FDR does not apply under such conditions.[3] If it comes down to deciding which gene exerts the tightest connection and highest clinical value, FDR might come in handy for multiple comparisons.

To summarize, in our published paper, Figure 7 is merely a further supplement of exploring the possible mechanism of LPCAT1 affecting survival in HCC patients. It simply presents the statistical significance between gene expression levels and survival rates, which is a single hypothesis test with only two factors, not multiple comparative screening of cancer biomarkers.

We would like to express our great gratitude again to the author for his attention to the article published by our team.

Conflict of interests

The authors declare that no conflict of interests exists.

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References

1. Zhang H, Xu K, Xiang Q, et al. LPCAT1 functions as a novel prognostic molecular marker in hepatocellular carcinoma. *Genes Dis*. 2022;9(1):151—164.
2. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J Royal Stat Soc Ser B Methodol*. 1995;57(1):289—300.
3. Curran-Everett D. Multiple comparisons: philosophies and illustrations. *Am J Physiol Regul Integr Comp Physiol*. 2000;279:R1—R8.

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