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Author Response Open Access

Article Title: New Score Tests for Equality of Variances in the Application of DNA Methylation Data Analysis

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Author Response

The followings are point-to-point responses to reviewers' comments and suggestions:

Reviewer: Wuyi Liu, Fuyang Normal University, China: I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
Response: Many thanks!

Reviewer: Yanghua He, Department of Animal and Avian Sciences, University of Maryland, USA
In this study, you evaluated the performance of the AWvar test and proposed three improved AWvar tests for DNA methylation data analysis, which may help identify DNA methylation marks that could potentially uncover the molecular differences between diseased samples and normal samples.
Response: Many Thanks!

1. Why do you choose AWvar test for DNA methylation data analysis? What are advantages of this test for DNA methylation data?

Response: Thanks for pointing out this! We clarified the motivations for studying the AWvar test in Abstract and in Introduction sections: (1) the joint test has good performance, and (2) the score tests of logistic regressions do not have distributional assumption for predictors. Hence, we expect the AWvar test would be robust to outliers and the violation of normality assumption. However, the performance of AWvar test has not been evaluated in the literature, we therefore investigated it in our manuscript.

2. For the event of DNA methylation, it usually occurs on CpG island regions. There are some linkages between single CpG sites inside of CpG islands. How do you consider this situation?

Response: Thanks for pointing out this! We totally agree that the correlations among CpG sites within the same CpG island would help improve the testing power. In this revision, we added this in Discussion section and will investigate how to utilize the correlation information in future study.

3. How do you think different methylation levels at single CpG sites between case and control samples caused by genetic variations such as SNPs?

Response: Thanks for pointing out this! Our QC and preprocessing steps have excluded CpG sites residing on SNPs. In this revision, we explicitly mention this at the end of the 1st paragraph of the section “Real data analyses”.

4. Your method may help for calling peaks that could be positive DNA methylation regions. Please extend the significance of your study in the Discussion Part.

Response: Thanks for the suggestion! We added this to the Discussion Part.