Professor George C. Prendergast

Editor-in Chief

*Cancer Research (CR)*

June 5, 2014

Dear Professor Prendergast,

Enclosed please find out our recent research paper entitled “Identification and validation of the methylation biomarkers of Non-small cell lung cancer (NSCLC)”. Currently, DNA methylation has been considered one of most promising biomarkers for early detection for NSCLC. A panel of appropriate methylation signature would significantly increase the survival time of NSCLC when NSCLC could be diagnosis in the early stage. However, the present methylation diagnosis panel was not power enough for clinical implement, which is because the biomarker combination is not optimized with effective statistic/discovery pipeline. In present study, we integrated 3 public DNA methylation microarray dataset (458 samples) and identified an optimized panel including 5 biomarkers (AGTR1, GALR1, SLC5A8, ZMYND10 and NTSR1) for the diagnosis of NSCLC. The diagnosis performance was validated in 150 paired NSCLC and normal tissues. Eventually, we demonstrate these 5 biomarkers would be an effective methylation-based assay for the NSCLC diagnosis, in which the accuracies were 98.98% and 90.93% in the train and validation stage, respectively, with 5-fold cross-validation. Our present study demonstrate that integrated analysis of multiple-platform high throughput DNA methylation microarray datasets followed by batch effect elimination could be taken as a good approach to discover diagnostic biomarker panels for NSCLC. We proposed a novel DNA methylation signature of AGTR1, GALR1, SLC5A8, ZMYND10 and NTSR1, which would be an effective methylation-based assay for the NSCLC diagnosis. I would greatly appreciate could you consider its suitability for publication in Cancer Research (CR).

All authors have agreed the current version of the manuscript. The manuscript has not been submitted to elsewhere for considering publication.

Thanks for your editorial help in advance.

Sincerely,

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