May 14st,2018

Dear editor:

I would like to submit a manuscript titled ‘Identification of hyper-methylated tumor suppressor genes-based diagnostic panel for esophageal squamous cell carcinoma (ESCC) in a Chinese Han population’ for possible publication in Frontiers in Genetics.

DNA methylation-based biomarkers have been suggested to be promising for early cancer diagnosis. However, a limited number of DNA methylation-based biomarkers for esophageal squamous cell carcinoma (ESCC), especially in Chinese Han populations have been identified and evaluated quantitatively. To search for the early diagnostic biomarkers for ESCC, candidate tumor suppressor genes (N = 65) were selected through literature searching, and four public high-throughput DNA methylation microarray datasets including 136 samples totally were collected for initial confirmation. Targeted bisulfite sequencing was applied in an independent cohort of 94 pairs of ESCC and normal tissues from a Chinese Han population for eventual validation. In summary, four candidate genes (ADHFE1, EOMES, SALL1 and TFPI2) were identified and validated in the ESCC samples from a Chinese Han population. All four candidate regions were validated to be significantly hyper-methylated in ESCC samples (ADHFE1, p = 1.70×10-3; EOMES, p = 2.90×10-9; SALL1, p = 3.90×10-7; TFPI2, p = 3.40×10-6). Logistic regression based prediction model shown a robust ESCC classification performance (Sensitivity = 66%, Specificity = 87%, AUC = 0.81). Moreover, advanced classification method had better performances (random forest and naive Bayes). Interestingly, the diagnostic performance could be improved in non-alcohol use subgroup (AUC = 0.84). In conclusion, we believed that methylation panels of ADHFE1, EOMES, SALL1 and TFPI2 could be an effective methylation based assay for ESCC diagnosis.  
  
I would greatly appreciate could you consider its suitability for publication in Frontiers in Genetics.  
  
  
Sincerely,

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