Dear Prof. Tsokos,

I want to make a presubmission inquiries to publish our present manuscript to XX. The manuscript is titled as “Aberrant methylation of CDH13 can be a diagnostic biomarker for lung adenocarcinoma”. We wish to be considered for publication in “xx” as an article.

Aberrant methylation of CpG islands in tumor cells in promoter regions is important in non-small cell lung carcinoma (NSCLC) tumorigenesis and a potential diagnostic biomarker for NSCLC patients. Previous reports have detected the existence of hypermethylation and loss of function of CDH13 in lung cancer, while the quantitative assessment of the diagnostic performance of CDH13 methylation status in NSCLC was unclear. The present study reviewed systemically and quantitatively the diagnostic ability of CDH13 methylation in NSCLC, as well as in its subsets, mainly adenocarcinoma and squamous cell carcimona, through meta-analysis (14 studies and 2109 samples) and four methylation microarray datasets from TCGA and GEO. The pooled odds ratio of CDH13 promoter methylation in cancer tissue from 2800 NSCLC samples was 6.06 (95% CI: 4.45 to 8.26, P < 0.00001) compared with that in controls. In validation stage, 126 paired samples from TCGA were analyzed and significant hypermethylation were confirmed in lung adenocarcinoma tissues but not in squamous cell carcinoma tissues. Concordantly, the results of other three datasets from GEO, consisting of 568 tumors and 256 normal tissues, also supported our previous findings. After combining all the microarray data above, The AUCs of logistic regression models based on the CpG site was 0.83-0.93 for Ad and 0.60-0.75 for SqC. In conclusion, the pooled data showed that the methylation status of the CDH13 promoter is strongly associated with lung adenocarcinoma, and thus the CDH13 methylation status could be a promising diagnostic biomarker for it.

All authors have read and approved this version of the article to be published, and due care has been taken to ensure the integrity of the work. No part of this paper has been published or submitted previously, and not under consideration for publication elsewhere, in whole or in part. We deeply appreciate your consideration of our manuscript. If you have any queries, please do not hesitate to contact me.