Dear Prof. Tsokos,

I want to make a pre-submission 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. Researchers have reported that hyper-methylation and loss of function of CDH13 were detected in lung cancer. However, the quantitative assessment of the diagnostic performance of the methylation status of CDH13 in NSCLC was not investigated yet. The present study systemically and quantitatively reviewed the diagnostic ability of CDH13 methylation in NSCLC as well as in its subsets through meta-analysis as well as four methylation microarray datasets from TCGA and GEO. The pooled odds ratio of CDH13 promoter methylation in cancer tissue 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 showed significantly hyper-methylation in lung adenocarcinoma tissues but not in squamous cell carcinoma tissues. Concordantly, the results from other three datasets, consisting of 568 tumors and 256 normal tissues, confirmed the previous findings. In conclusion, the pooled data showed that the methylation status of the CDH13 promoter is strongly associated with lung adenocarcinoma. The CDH13 methylation status could be a promising diagnostic biomarker for diagnosis of lung adenocarcinoma.

All authors have read and approved this version of the article, and due care has been taken to ensure the integrity of the work. The manuscript is approved by all authors for publication. 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, and we look forward to receiving comments from reviewers. If you have any queries, please do not hesitate to contact me.