Comments to the Editor,

This manuscript studied the quantitative mRNA and DNA methylation profile of three tumor suppressor genes which located in the famous LUCA region in Non-small cell lung cancer in a large Poland population. In the present study, the DNA methylation and gene expression of FUS1, NPRL2/G21 and RASSF1A were measured in same lung cancer and adjacent tissues simultaneously, meanwhile, the gene expression level of DNMT1 and DNMT3B were also detected with RT-PCR. And the relationship among gene expression, DNA methylation and sample states (cancer, normal and/or subtype) were estimated with perfect statistic method. The study was performed rigorously and the findings are interesting. In general, I'd recommend publication if the authors can address the following concerns.

1, what’s the degree of the estimated LOH frequency of LUCA region in NSCLC and this should be provided in the background section.

2, Reference should be provided at line 39 of page 3.

3, Please provide the counts of the sample in each cell of Table 3.

4, why set RQ equal to 0.5 in Table 3, rather than other values?

5, How to determine the annealing temperature in the process of MSP?

6, the genomic position of CpG site in primers and the PCR production should be provided in the Table 2.

7, The font size of the legends in Figure 1 is too small.

8, Please change the Table 5 to a figure so that readers can get more information from the data.

9, Is there any evidence showed the mutation and the hypermethylation of these three genes can be considered as diagnostic biomarker for NSCLC? And Do you think the primer in present study can be used in the methylation detection in plasma samples?

10, why human fetal cell line could be taken as negative control? They do not have any methylation in such genomes?

11, Please provide the sensitivity, specificity with such three genes (DNA methylation or/and gene expression) in the prediction or distinguish of the NSCLC from normal tissues in result or discussion section.

12, Is there any possibility to discrete continuous MI to binary status (methylation or unmethylation), so that, the present data can be re-used in the future meta-analysis?

13, why the authors believe DNA methylation can be used as diagnostic biomarkers/models? Can you provide some lasted/promising diagnostic model or biomarkers which are based on DNA methylation in the background section? What’s the best diagnosis accuracy can be achieved by DNA methylation based biomarkers/models?