March 18, 2014

Dear Ms. Jera Mae Eluna,

Thank you for your letter on Mar 15, 2014 regarding our manuscript entitled “Quantitative assessment of the diagnostic role of APC promoter methylation in non-small cell lung cancer”. We have revised the manuscript following your comments and instructions; meanwhile we provide all the response to your comments as the following.

Best regards,

Jiucun Wang

**Response to the queries in the main body**

1. **ED Query: kindly request the alteration of the 1.5 gauge bold lines to ¾ gauge.**

Response: Thanks for your revision. We removed your comments from the manuscript to keep the format to be published.

ED Query: I have retained the bold type for selected numerals in the tables as this is specifically indicated by the authors. Kindly advise if alternative styling is preferred

Response: yes, bold type for selected numerals would be preferred, thank you for your help. We removed your comments from the manuscript to keep the format to be published.

1. “ED Query: I am unable to examine fig 2 as it has failed to download on my PC so kindly check that (A through F) are separate panels and therefore whether my use of bold for them here is appropriate.

Response: yes, they are separate panels and your bold operation is suitable. Thank you for your revision. We removed your comments from the manuscript to keep the format to be published.

1. {“AU Query: I am finding this last sentence section (from (P < 0.026) difficult to understand clearly. Kindly review and consider some alteration to rectify this.”}

Response: We replaced the previous sentence with the following so that readers can understand it clearly. “The sample type of tissue or serum would be one of the heterogeneity sources (P < 0.026) when Begum et al. ([12], US) were removed from the meta studies;”

1. {“AU Query: kindly check this last sentence for clarity of meaning following my alterations}

Response: yes, we agree with what you have done to the last sentence.

1. {“AU Query: kindly confirm that the first part of this sentence reads correctly regarding your intended message: possible the word ‘virtual’ may need reviewing. Please advise.”}

Response: maybe we can replace ‘Seven virtual studies’ with ‘Seven imputed studies’, I think it will be understand easily.

1. {“AU Query: kindly check that the amendments I have made, to try to improve clarity of the above few sentences, convey your intended messages accurately.”}

Response: yes, we agree with the amendments you have conducted. It is more accurate.

1. {“AU Query: I have integrated the last section of your Discussion into your Conclusion because both contain similar elements. Kindly advise if this is not acceptable.”}

Response: yes, you are quite right. We definitely agree with you. Thank you so much for the help.

**Response to the queries at the last page**

1. Author names: Please confirm the author names are presented accurately, and in the correct sequence (given names/initials, family name).

Response: only author 11 needs to be revised. Her given name is Jiucun not “Jiu-Cun”.

1. All additional files must be cited in ascending numerical order; however, the original sequence of citations 2 and 1 was out of order. All affected additional files were renumbered including their corresponding files. Please check if the action taken is appropriate. Otherwise, kindly advise us on how to proceed.

Response: yes, the action is appropriate. Thank you so much.

1. Supplementary Table citations were changed to Additional file 1: Table S1-S5Supplementary Figure citations were changed to Additional file 2: Figure S1-S3 to avoid confusion with any figures and tables included within the main text. Moreover, titles inside the additional files were also amended to correspond with their modified citations. Please check if appropriate.

Response: Yes, the action is appropriate. Thank you so much.

1. Additional file 2 was mentioned in the manuscript; however, no e-file was provided. Please supply the e-file of the mentioned additional file. Otherwise, kindly advise us on how to proceed.

Response: Sorry, we have enclosed the additional file 2, please check it.

1. Competing interests: Journal instruction requires a “Competing interests” section; however, none was provided. The authors are required to complete a declaration of competing interests. All competing interests that are declared will be listed before the references. In this regard, please provide the missing section. Please note that if the authors give no competing interest, the listing should read as “The authors declare that they have no competing interests”.

Response: Sorry for that. All the authors have no competing interests. We have added this missing section before the references.

1. Citation details for Reference [9] are incomplete. Please supply the Volume number and Page range of this reference. Otherwise, kindly advise us on how to proceed.

Response: thank you for your remind. I added the volume and page information for this reference.

1. References 5, 6, 8-10, 12-24, 27, 28, 31-33, 35 and 41: Citations in the reference list should include all named authors, up to the first 30 before adding 'et al.'

Response: Sorry for that, but we prepared the citation definitely according to the endnote file which *Clinical Epigenetics* provided in your website. Anyway, we have changed the author list rules in which the first 30 authors are listed and then adding 'et al.'.