Author's response to reviews

Title: Non-Small Cell Lung Cancer with EML4-ALK Translocation in Chinese Male Never-Smokers is Characterized with Early-Onset

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Version: 8 Date: 5 October 2014

Author's response to reviews: see over
Dear Dr. Dafne Solera or editor of the *BMC Cancer*

We would like to thank you for considering our manuscript (MS: 4124372561153266) entitled “Non-Small Cell Lung Cancer with *EML4-ALK* Translocation in Chinese Male Never-Smokers is Characterized with Early-Onset” as potentially suitable for publication in the *BMC Cancer* and inviting us to resubmit it with revision. In the revised manuscript enclosed, we have fully addressed the reviewers' concerns, as detailed below in the section “Response to the Reviewers’ Comments”. Having made these changes, we respectfully request that the revised manuscript be accepted for publication in the *BMC Cancer*.

Sincerely,

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**Response to the Reviewers’ Comments:**

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NOTE: In this round of review, two reports were provided to us, from Reviewers #1 and #2.

**Reviewer 1 (Haruhiko Sugimura)**

Mandatory request:

1. Please test by the other method such as RT-PCR or FISH the fusion of this genes at least some of the cases of their cohort. Actually RT-PCRs are feasible test of this fused transcript. (*EML4-ALK* fusion transcripts in immunohistochemically ALK-positive non-small cell lung carcinomas. by Shinmura K, Kageyama S, Igarashi H, Kamo T, Mochizuki T, Suzuki K, Tanahashi M, Niwa H, Ogawa H, Sugimura H. Exp Ther Med. 2010 Mar;1(2):271-275. Epub 2010 Mar 1.)

Response: We used suggested methods (with reference cited) to verify our RT-PCR and revised the Methods and Results sections accordingly:

We added “RT-PCR was also performed using a different set of primers that were previously published [24].” in the Methods (2\(^{nd}\) paragraph) and “These results were verified by additional RT-PCR experiments using a set of previously published primers [24].” in the Results (2\(^{nd}\) paragraph).

2. Provide the significance of this high prevalence and possible influence on the treatment strategy of lung cancer patients in your region.

Response: We made changes to emphasize local influence in the 5\(^{th}\) paragraph of the Discussion section.

**Reviewer 2 (Maria Wong)**

Discretionary Revision

Does the tumour shown in Fig 4C show ALK expression? This figure is added in response to one of the reviewers' comments that ALK translocation adenocarcinomas are more likely to harbour a mucinous cribriform pattern and yet this feature is not shown on the IHC photo (Fig 4C) or tabulated results (Table 4) and therefore does not illustrate the intended purpose.

Response: We have replaced Fig. 4C with new Fig. 4C and 4D (ALK staining was shown in Fig. 4D) and revised the legend accordingly. We also updated Table 4 by indicating the carcinomas with mucinous cribriform pattern.