The Author Response

EML4-ALK Fusion Gene in Korean Non-Small Cell Lung Cancer

Jae Yong Park

Department of Biochemistry and Cell Biology, and Internal Medicine, Kyungpook National University School of Medicine, Daegu, Korea

I would like to thank the interest and comments on our paper entitled “EML4-ALK fusion gene in Korean non-small cell lung cancer” (1). In this study, we examined EML4-ALK fusion variants in Korean non-small cell lung cancers (NSCLCs) via reverse-transcriptase-polymerase chain reaction (RT-PCR) using primers designed to detect EML4-ALK fusion variants (variants 1, 2, 3a, 3b, 4, 5a, 5b, 6, and 7) that have been previously identified (2, 3). Our study demonstrated the spectrum and frequency of EML4-ALK fusion variants in Korean NSCLCs, which were different from those in other ethnic populations.

I agree with the comment that the RT-PCR technology for identification of ALK fusion variants has several limitations. As pointed out in this comment, there are multiple EML4-ALK fusion partners and non-EML4 fusion partners, such as KIF5B, and KLC1 (2-5); therefore, any PCR-based strategy must incorporate validated primer pairs for all known ALK fusions. Another limitation is that given that most specimens from lung cancer patients are stored as formalin-fixed paraffin embedded tissue, the RNA may have been substantially degraded relative to non-fixed, fresh-frozen tissue. In addition, it has been reported that PCR-based detection of EML4-ALK can yield positive results in the absence of detectable ALK-rearrangement in both tumor and non-tumor tissues, suggesting a propensity for false positive results (6). The aim of our study was to examine the profile of known EML4-ALK fusion variants in Korean NSCLCs and was not to detect the presence of ALK fusion to other gene partners. The limitations of the RT-PCR analysis, such as the necessity of available high-quality RNA and the propensity of false positive results, were briefly discussed in the paper. I agree with the suggestion that long-distance-PCR or long distance inverse-PCR could be used to identify all EML4-ALK fusion variants as well as other ALK rearrangements having known or even unknown fusion partner genes (7, 8).

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Address for Correspondence:
Jae Yong Park, MD
Lung Cancer Center, Kyungpook National University Medical Center, 807 Hoguk-ro, Buk-gu, Daegu 702-210, Korea
Tel: +82.53-200-2631, Fax: +82.53-200-2027
E-mail: jaeyong@knu.ac.kr

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