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The Author Response

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

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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 variants 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).

REFERENCES

1. Jin G, Jeon HS, Lee EB, Kang HG, Yoo SS, Lee SY, Lee JH, Cha SI, Park TI, Kim CH, et al. *EML4-ALK fusion gene in Korean non-small cell lung cancer. J Korean Med Sci 2012; 27: 228-30.*
2. Sasaki T, Rodig SJ, Chirieac LR, Jänne PA. *The biology and treatment of EML4-ALK non-small cell lung cancer. Eur J Cancer 2010; 46: 1773-80.*
3. Horn L, Pao W. *EML4-ALK: honing in on a new target in non-small-cell lung cancer. J Clin Oncol 2009; 27: 4232-5.*
4. Takeuchi K, Choi YL, Tagashi Y, Soda M, Hatano S, Inamura K, Takada S, Ueno T, Yamashita Y, Satoh Y, et al. *KIF5B-ALK, a novel fusion oncokinases identified by an immunohistochemistry-based diagnostic system for ALK-positive lung cancer. Clin Cancer Res 2009; 15: 3143-9.*
5. Togashi Y, Soda M, Sakata S, Sugawara E, Hatano S, Asaka R, Nakajima T, Mano H, Takeuchi K. *KLC1-ALK: a novel fusion in lung cancer identified using a formalin-fixed paraffin-embedded tissue only. PLoS One 2012; 7: e31323.*
6. Martelli MP, Sozzi G, Hernandez I, Pettirossi V, Navarro A, Conte D, Gasparini P, Perrone F, Modena P, Pastorino U, et al. *EML4-ALK rearrangement in non-small cell lung cancer and non-tumor lung tissues. Am J Pathol 2009; 174: 661-70.*
7. Kim MJ, Cho SY, Kim MH, Lee JJ, Kang SY, Cho EH, Huh J, Yoon HJ, Park TS, Lee WI, et al. *FISH-negative cryptic PML-RARA rearrangement detected by long-distance polymerase chain reaction and sequencing analysis: a case study and review of the literature. Cancer Genet Cytogenet 2010; 203: 278-83.*
8. Meyer C, Schneider B, Reichel M, Angermueller S, Strehl S, Schnittger S, Schoch C, Jansen MW, van Dongen JJ, Pieters R, et al. *Diagnostic tool for the identification of MLL rearrangements including unknown partner genes. Proc Natl Acad Sci U S A 2005; 102: 449-54.*

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