The development of a highly sensitive mouse monoclonal antibody for screening ALK-rearrangements in lung cancers

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Abstract

The anaplastic lymphoma kinase (ALK) rearrangements, mostly EML4-ALK fusion, occur in 3-7% of lung cancer patients and define a patient population that could respond to receptor tyrosine kinase inhibitor Crizotinib and Ceritinib. Currently, ALK testing is mostly conducted by either fluorescence in situ hybridization (FISH) or polymerase chain reaction (PCR) methods, either of which has its own limitations. The detection of the ALK protein in lung cancer patient tissues by IHC was found to be difficult mostly due to the low abundance of its fusion product. To overcome this limitation, we have developed an ALK mouse monoclonal antibody (clone 1A4) that is more sensitive than a current rabbit ALK antibody DSF3. Our initial analyses revealed that 1A4 can correctly identify all 5 EML4-ALK positive samples that were previously confirmed by QPCR tests, while did not yield significant background on all 30 EML4-ALK negative lung cancer samples. By using a different IHC detection system, we further tested 1A4 on 17 ALK-positive and 10 ALK-negative lung cancer biopsy specimens that have been validated by either FISH or PCR from another hospital. The IHC result of the antibody 100% agreed with the previous molecular diagnosis. The high concordance of the IHC results by the novel ALK antibody with other DNA/RNA based detection methods suggested that 1A4 could be used routinely for screening ALK-rearrangement genetic events among patients.

Background

Generating an ALK IHC antibody

Comparison between 1A4 and DSF3

1A4 staining and ALK FISH results

More sensitive ALK antibody cocktails

References


Lung cancer and different forms of ALK translocation. (A). Top 20 human cancer type around the world. Lung cancer is the most frequent cancer type [WCRF, 2008] (B). Top oncogenic molecular mutations in lung adenocarcinomas. (C). Schema of ALK fusion protein resulted from ALK translocations and representative ALK translocation events in lymphomas and lung cancer. (D). Frequency of different EML4-ALK translocation varieties reported in NSCLC.