

Novel assay developed for detecting ALK rearrangement in NSCLC

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Researchers have developed a novel technique for detecting ALK rearrangements in non-small cell lung cancers (NSCLCs) that is more sensitive and easier to perform than currently available techniques. The technique can help enhance the routine practice of diagnostic ALK testing on NSCLCs, which is crucial for identifying patients with advanced NSCLC who are most likely to benefit from targeted therapy with an ALK inhibitor.

None of the current three routine methods used to detect ALK rearrangements in NSCLC is without drawbacks, especially for tissue specimens that are fixed in formalin and embedded in paraffin. Fluorescent in situ hybridization (FISH) is the only approved technique for ALK testing, but it is not always feasible because of high cost, the time required for testing, and the need for specialized equipment and expertise. Interpretation of immunohistochemistry (IHC) results can be challenging because of weak and variable immunoreactivity. Reverse transcription-polymerase chain reaction (RT-PCR) is highly sensitive, but requires high-quality RNA, which is often difficult to obtain, and cannot detect rearrangements with unknown partners.

The novel technique, based on quantitative (q)RT-PCR, overcomes these issues by capitalizing on the sensitivity of RT-PCR and including two features: an RNA isolation method that was optimized to reverse formaldehyde modification and small RT-PCR amplicons to allow for the use of fragmented nucleic acids for efficient amplification of ALK cDNA. The novel qRT-PCR test measures the expression of the 5' and

the 3' portions of the ALK transcript separately; it detected unbalanced ALK expression indicative of a gene rearrangement in 24 (4.6%) of 523 interpretable NSCLC specimens and full-length ALK transcript expression in six tumors (1.1%). Both FISH and qRT-PCR testing were done on 182 tumors; qRT-PCR accurately typed 97% of 19 tumors with ALK rearrangements and 158 with no rearrangements. The findings of the study are published in the March issue of the *Journal of Thoracic Oncology* (JTO), the official journal of the International Association for the Study of Lung Cancer (IASLC).

"The qRT-PCR technique reliably detects ALK-rearranged tumors independently of the fusion partner and also identifies tumors with full-length transcript expression of the gene that is not detectable by FISH but may be relevant for ALK inhibitor therapy as well," says lead author Claudia Kalla, PhD, of the Department of Clinical Pathology, Robert-Bosch-Krankenhaus and the Dr. Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart, Germany. "The technique seems to be a sensitive, easy-to-perform, and high-throughput method suitable for the routine diagnosis of ALK activation not only in lung cancer, but also in other tumor entities where rearrangements with alternative fusion partners or transcriptional upregulation are prevalent."

Provided by International Association for the Study of Lung Cancer

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