Detection of NTRK1/2/3 rearrangements by PCR test for 5'/3'-end unbalanced expression


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BACKGROUND

NTRK1, NTRK2 and NTRK3 rearrangements are rare genetic events, which are difficult to detect due to diversity of translocation partners and varying position of break-points.

METHODOLOGY

We assumed that the fusion-driven activation of the NTRK1/2/3 results in the overexpression of the kinase portion of the involved gene, and developed a PCR assay which evaluates the ratio between 5'- and 3'- ends of the NTRK1, NTRK2 and NTRK3 transcripts in the tumor cDNA. The identity of translocation variants in tumors with unbalanced 5'/3'-end expression was established by allele-specific PCR tests (Figure 1) or next-generation sequencing (NGS) (Figure 2).

RESULTS

NTRK1/2/3 rearrangements were detected in 6/5102 (0.12%) consecutive non-small cell lung carcinomas (NSCLCs). All these NTRK fusions were represented by distinct variants and were present in patients of distinct gender and age.

In contrast to low frequency in NSCLCs, there was a noticeable occurrence of NTRK1/2/3 rearrangements in pediatric tumors (9/93, 9.7%), salivary gland carcinomas (3/85, 3.5%) and microsatellite-unstable colorectal cancers (3/33, 9.1%). While there was a diversity of the translocation variants in NSCLCs, more than a half of NTRK fusions detected in non-NSCLC tumors were represented by the ETV6ex5/NTRK3ex15 chimera.

CONCLUSION

PCR test for 5'/3'-end unbalanced expression is a cost-efficient screening tool for NTRK1/2/3 rearrangements.

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