OPTIMIZING THE DETECTION OF GENOMIC ALTERATIONS, INCLUDING PATHOGENIC GENE FUSIONS

Conventional biomarker screening does not detect the full breadth of genomic alterations

Tests such as RT-PCR, FISH, and IHC were developed to detect single molecular targets.[1,2]

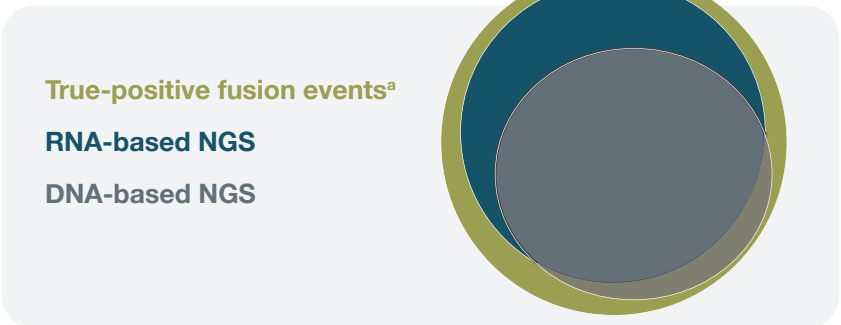
These methods may be unable to identify the full breadth of genomic alterations, fusion partners, and breakpoints, and risk exhausting tissue samples due to the high amounts needed for sensitivity.[1-4]

NGS can detect a broad range of genomic alterations[5]

NGS is a high-throughput genomic sequencing technology that allows for the simultaneous analysis of numerous alterations; NGS can be DNA-based, RNA-based, or both[1,6]

NGS process[7]

DNA-based NGS alone can miss pathogenic gene fusions[8]



DNA-based sequencing can lead to false-negative and false-positive results in a variety of cases, particularly in detection of gene fusions[8,9]

[a]Graphic for illustrative purposes only. Not drawn to scale or reflective of actual results captured by different methodologies.

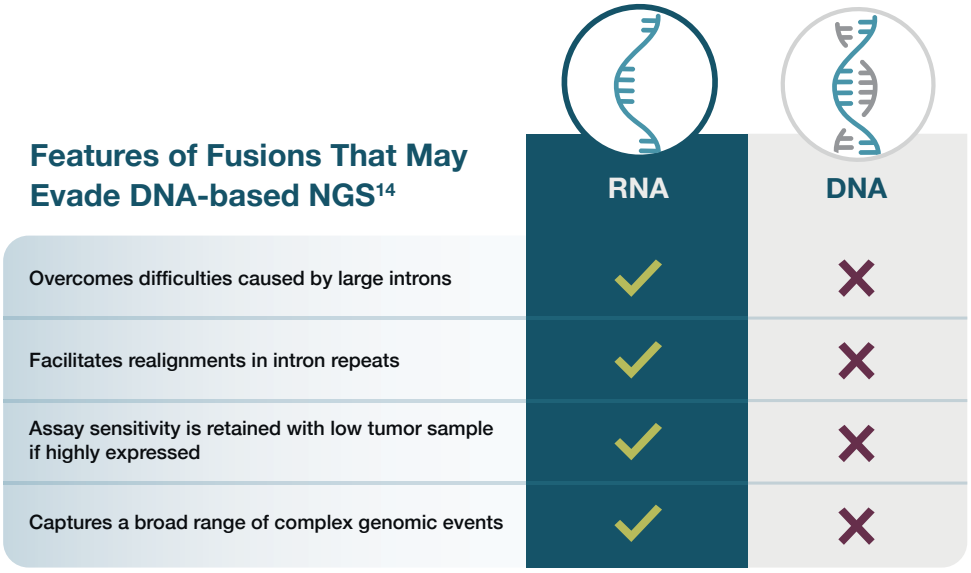
Comprehensive testing with RNA-based NGS, including DNA and RNA sequencing, is recommended to capture what DNA-based NGS alone can miss[1,8]

FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; NGS, next-generation sequencing; RT-PCR, reverse transcription-polymerase chain reaction.

Why is RNA-based NGS more comprehensive in detecting pathogenic gene fusions?[10]

RNA-based NGS

- Detects gene expression and structural variants[11]
- Reduces many of the technical challenges involved in sequencing long introns[11]
- Enables oncologists to match therapy to the driving fusion—which wouldn't have otherwise been identified—potentially leading to improved clinical responses[8,12,13]



NRG1: A dangerous pathogenic gene fusion

- *NRG1* is particularly challenging to detect without RNA-based NGS due to its diversity of gene fusion partners and breakpoints and its large intronic region[15]
- A retrospective study at Memorial Sloan Kettering Cancer Center included 30 patients with *NRG1*+ tumors who had both DNA-based and RNA-based NGS performed. Of these, 28 were identified by RNA-based NGS but were undetected by DNA-based NGS[10]

Please visit **www.FindTheFusions.com** to learn more

NGS, next-generation sequencing; *NRG1*, neuregulin 1; *NRG1*+, neuregulin 1 fusion positive.

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