

OPTIMIZING THE DETECTION OF GENOMIC ALTERATIONS, INCLUDING PATHOGENIC GENE FUSIONS

Conventional test methods limit the ability to detect many pathogenic gene fusions

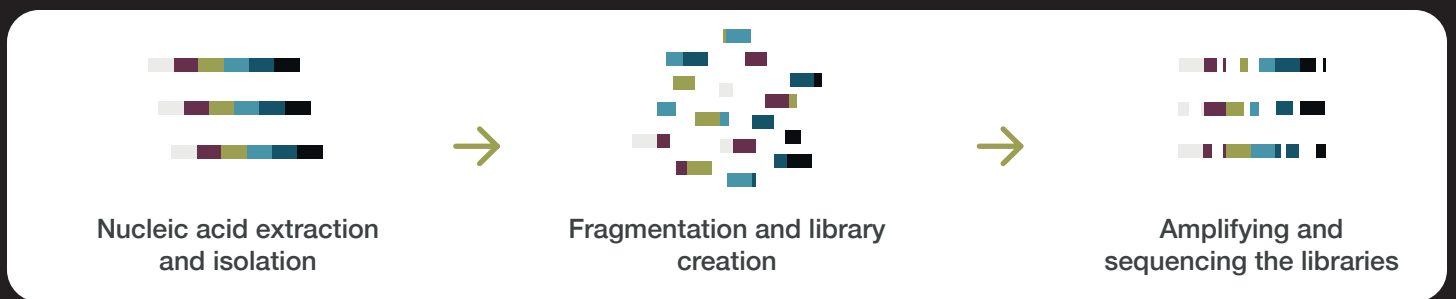


Tests such as RT-PCR, FISH, and IHC were developed to detect single molecular targets.^{1,2} These methods may be unable to identify the full breadth of genomic alterations, fusion partners, and breakpoints, and risk exhausting tissue samples due to the high amounts needed for sensitivity.¹⁻⁴

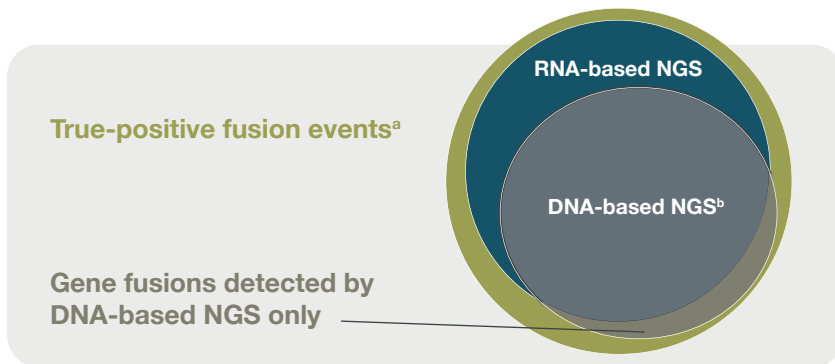
NGS can detect a broad range of genomic alterations⁵

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 process⁷



DNA-based NGS alone can miss pathogenic gene fusions⁸



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

^aGraphic for illustrative purposes only. Not drawn to scale or reflective of actual results captured by different methodologies.



^bDNA-based NGS can detect some fusions not found by certain RNA-based NGS.⁹

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

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

RNA-based NGS

- Detects gene expression and many structural variants¹¹
- Reduces many of the technical challenges involved in sequencing long introns¹¹
- 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}

Features of Fusions That May Evade DNA-based NGS ¹⁴	 RNA	 DNA
	Overcomes difficulties caused by large introns	✓
Facilitates realignments in intron repeats	✓	✗
Assay sensitivity is retained with low tumor sample if highly expressed	✓	✗
Captures a broad range of complex genomic events	✓	✗

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 region¹⁵
- 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 NGS¹⁰

Please visit www.FindTheFusions.com to learn more

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

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