

# OPTIMIZING THE DETECTION OF GENOMIC ALTERATIONS, INCLUDING PATHOGENIC GENE FUSIONS

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

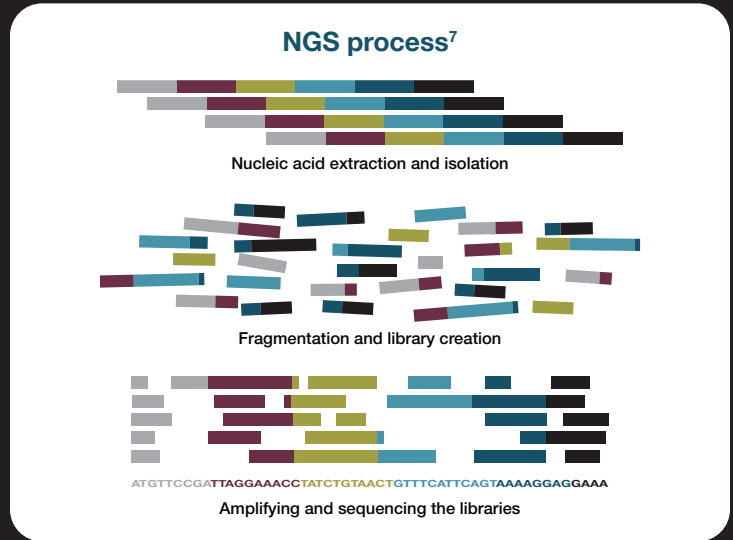


Tests such as RT-PCR, FISH, and IHC were developed to detect single molecular targets.<sup>1,2</sup>

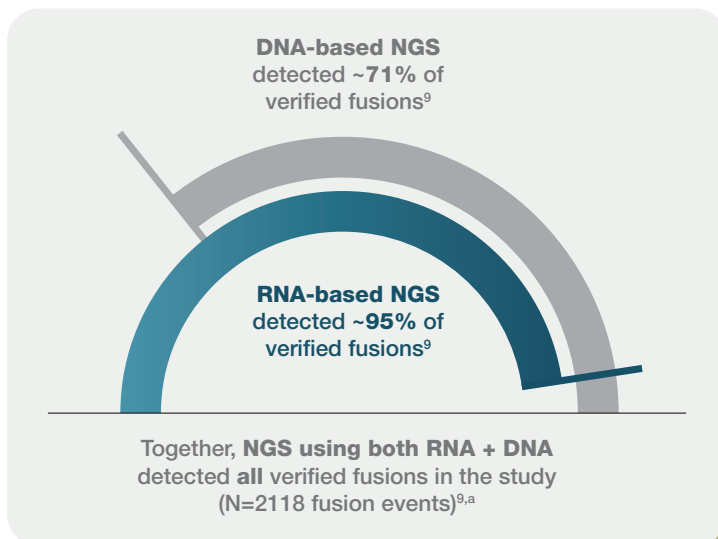
These methods may be unable to identify the full breadth of genomic alterations, fusion partners, and breakpoints, and risk exhausting tissue samples due to the high amounts needed for sensitivity.<sup>1-4</sup>

## NGS can detect a broad range of genomic alterations<sup>5</sup>

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.<sup>1,6</sup>



## DNA-based NGS alone can miss pathogenic gene fusions<sup>8</sup>



DNA-based sequencing can lead to false-negative and false-positive results in a variety of cases, particularly in the detection of gene fusions.<sup>8,10</sup>

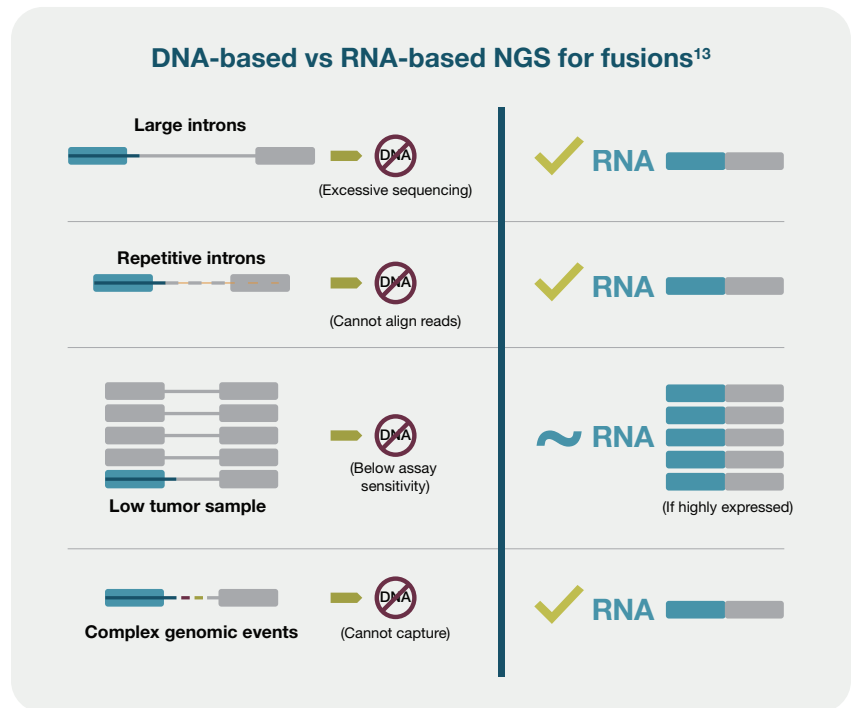
**Comprehensive testing with RNA-based NGS, including DNA and RNA sequencing, is recommended to capture what DNA-based NGS alone can miss<sup>1,8</sup>**

<sup>a</sup>Based on NGS testing of tissue samples.<sup>9</sup>

# Why is RNA-based NGS more comprehensive in detecting pathogenic gene fusions?<sup>11</sup>

## Advantages of RNA-based NGS

- Detects gene expression and many structural variants<sup>12</sup>
- Reduces many of the technical challenges involved in sequencing long introns<sup>12</sup>
- Can improve the detection rate of DNA-based NGS alone and provide more comprehensive detection results<sup>13</sup>
- Enables oncologists to match therapy to the driving fusion—which wouldn't have otherwise been identified—potentially leading to improved clinical responses<sup>8,14,15</sup>



## 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<sup>16</sup>
- A retrospective study at Memorial Sloan Kettering Cancer Center included 34 samples from 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<sup>11</sup>

Please visit [www.FindTheFusions.com](http://www.FindTheFusions.com) to learn more

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

**References:** 1. Bruno R, Fontanini G. Next generation sequencing for gene fusion analysis in lung cancer: a literature review. *Diagnostics (Basel)*. 2020;10(8):521. doi:10.3390/diagnostics10080521 2. Su D, Zhang D, Chen K, et al. High performance of targeted next generation sequencing on variance detection in clinical tumor specimens in comparison with current conventional methods. *J Exp Clin Cancer Res*. 2017;36(1):121. doi:10.1186/s13046-017-0591-4 3. Next-generation sequencing testing in oncology. Personalized Medicine in Oncology. Accessed March 26, 2026. <https://www.jons-online.com/special-issues-and-supplements/2020/faculty-perspectives-next-generation-sequencing-testing-in-oncology-part-4-of-a-4-part-series/next-generation-sequencing-testing-in-oncology> 4. Yu TM, Morrison C, Gold EJ, Tradonsky A, Layton AJ. Multiple biomarker testing tissue consumption and completion rates with single-gene tests and investigational use of oncomine Dx target test for advanced non-small-cell lung cancer: a single-center analysis. *Clin Lung Cancer*. 2019;20(1):20-29.e8. doi:10.1016/j.clcc.2018.08.010 5. Singh RR. Next-generation sequencing in high-sensitive detection of mutations in tumors: challenges, advances, and applications. *J Mol Diagn*. 2020;22(8):994-1007. doi:10.1016/j.jmoldx.2020.04.213 6. Goswami RS, Luthra R, Singh RR, et al. Identification of factors affecting the success of next-generation sequencing testing in solid tumors. *Am J Clin Pathol*. 2016;145(2):222-237. doi:10.1093/ajcp/aqv023 7. ABM Inc. Next generation sequencing (NGS) - data analysis. Accessed March 24, 2026. [https://old.abmgood.com/marketing/knowledge\\_base/next\\_generation\\_sequencing\\_data\\_analysis.php](https://old.abmgood.com/marketing/knowledge_base/next_generation_sequencing_data_analysis.php) 8. Benayed R, Offin M, Mullaney K, et al. High yield of RNA sequencing for targetable kinase fusions in lung adenocarcinomas with no mitogenic driver alteration detected by DNA sequencing and low tumor mutation burden. *Clin Cancer Res*. 2019;25(15):4712-4722. doi:10.1158/1078-0432.CCR-19-0225 9. Michuda J, Park BH, Cummings AL, et al. Use of clinical RNA-sequencing in the detection of actionable fusions compared to DNA-sequencing alone. *J Clin Oncol*. 2022;40(16):3077. doi:10.1200/JCO.2022.40.16 10. Heydt C, Wölwer CB, Velazquez Camacho O, et al. Detection of gene fusions using targeted next-generation sequencing: a comparative evaluation. *BMC Med Genomics*. 2021;14(1):62. doi:10.1186/s12920-021-00909-y 11. Benayed R, Liu SV. Neuregulin-1 (*NRG1*): an emerging tumor-agnostic target. Clinical Care Options. Accessed March 24, 2026. <https://deceraclinical.com/education/activity/ecase/B512CF6E-75C3-41DC-88B2-40156A42BE70/1> 12. Mahmoud M, Gobet N, Cruz-Dávalos DI, Mounier N, Dessimoz C, Sedlazeck FJ. Structural variant calling: the long and the short of it. *Genome Biol*. 2019;20(1):246. doi:10.1186/s13059-019-1828-7 13. Davies KD, Aisner DL. Wake up and smell the fusions: single-modality molecular testing misses drivers. *Clin Cancer Res*. 2019;25(15):4586-4588. doi:10.1158/1078-0432.CCR-19-1361 14. Cobain EF, Wu Y-M, Vats P, et al. Assessment of clinical benefit of integrative genomic profiling in advanced solid tumors. *JAMA Oncol*. 2021;7(4):525-533. doi:10.1001/jamaoncol.2020.7987 15. Hindi I, Shen G, Tan Q, et al. Feasibility and clinical utility of a pan-solid tumor targeted RNA fusion panel: a single center experience. *Exp Mol Pathol*. 2020;114:104403. doi:10.1016/j.yexmp.2020.104403 16. Drilon A, Duruisseaux M, Han J-Y, et al. Clinicopathologic features and response to therapy of *NRG1* fusion-driven lung cancers: the eNRGy1 Global Multicenter Registry. *J Clin Oncol*. 2021;39(25):2791-2802. doi:10.1200/JCO.20.03307